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INTRODUCTION OF NEW DRUGS

THE joint report on thiouracil by pharmaceutical manufacturers and the Food and Drug Administration, reproduced elsewhere in this issue, represents a significant and welcome development in the method of introducing new drugs.

Like many new drugs, thiouracil is not only more effective but also more toxic and difficult to administer properly than most time-honored remedies on the pharmacist's shelves. Release of thiouracil for general use against hyperthyroidism was justifiably delayed for some time because of fears of too frequent toxic reactions.

Some of us are impatient when new drugs do not immediately become available after promising clinical trials have been widely publicized. But are we willing to share with physicians the responsibility for proper dosage, and for possibly tragic untoward reactions, by dispensing new drugs before a solid foundation of clinical experimentation has been established?

It can hardly be questioned that the release of new drugs must sometimes be delayed unduly because clinical investigations are not sufficiently coordinated; because the results of independent investigations sponsored by competing manufacturers too often are not correlated for the benefit of all. The new Therapeutic Trials Committee established by the American Medical Association has an excellent opportunity to improve the coordination and planning of clinical trials. The joint report on thiouracil by manufacturers and the FDA points the way toward helpful correlation of data obtained.

In the case of thiouracil, each of 6 pharmaceutical manufacturers had submitted a new drug application to the FDA. Buried in these applications was evidence that much information on the safe administration of the drug was available but unreported. The FDA wisely brought the drug manufacturers together on a plan to pool their data and conduct a survey of results obtained by clinicians.

Here now was the basis on which the drug could be evaluated properly and released for general use. The remaining problem was to get this information on indications, dosage and precautions into the hands of physicians and pharmacists when the drug was released. At a conference held under the auspices of the Food and Drug Administration, the medical directors of the pharmaceutical manufacturers and a representative of the American Medical Association agreed that the pooled data should be made available to the medical profession as a report to the A. M. A.'s Council on Pharmacy and Chemistry. We present the report for pharmacists through the cooperative arrangement between the Council on Pharmacy and Chemistry and the A. PH. A. which brings Council reports and data on Council accepted products to you regularly in THIS JOURNAL.

This report, the first of its kind, marks a milestone in cooperation. We hope that thiouracil represents only the first instance of many in which information reported in new drug applications will be correlated and evaluated for use by physicians and pharmacists.

INFORMATION WANTED

IF properly applied, current labeling regulations of the FDA should win general approval. Drugs suitable for lay use will be adequately labeled; drugs for prescription use only will be clearly identified as such. At the same time it must be recognized that the absence of directions and especially dosage statements on newer prescription drugs is not without disadvantages and even dangers.

Some physicians seem disposed to prescribe merely on the basis of partial or preliminary clinical information found somewhere in the literature. Some pharmacists are filling prescriptions for drugs regarding which they do not have adequate information, even though they must share responsibility with the physician for proper dosage and administration.

Modern medical practice requires critical selection from an expanding armamentarium of drugs and information on pharmacology, toxic side effects and the regimen of new types of therapy.

Pharmacists who recognize today's trends are aware of the need for such information in providing a competent prescription service, as they fill the role of adviser to physicians on the multitude of new medications, and in safeguarding the patient.

Less time spent in compounding should mean more time spent with professional journals and the manufacturing pharmacist's literature—in evaluating and filing, mentally and manually, information on new drugs.

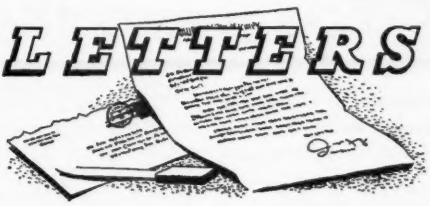
The appearance of many unfamiliar and potent products bearing the prescription legend puts emphasis on a new, or at least greatly expanded, function of the retail pharmacist.

WORKING TOGETHER FOR BETTER PHARMACY

Sirs:

In remitting my dues for 1946 I want to indicate my support of the ASSOCIATION'S activities . . . and to tell you what a good job I think you are doing.

I can think of no reason why a man would select a profession and then fail to do everything in his power to promote its best interests. Surely membership in the national association is the least that could be expected.



No doubt you are aware of the splendid work that Dr. L. David Hiner of Ohio State University has done in promoting A. PH. A. to students there. No serious-minded pharmacist or pharmacy student could hear him tell of the ASSOCIATION'S work, and its function in American pharmacy, and fail to become a member for life.

I joined while still a student . . . and am now engaged in retail pharmacy.

Dayton, O. ROBERT J. BIRMINGHAM

SOURCE OF TABLET AND CAPSULE MACHINES

Sirs:

Please give me the address of manufacturers of small tablet and capsule machines . . . .

San Antonio, Texas VOLNEY M. PLATT

Two principal suppliers of small-scale tablet machines are the F. J. Stokes Machine Co., 6002 Tabor Rd., Philadelphia, and the Arthur Colton Co., Detroit, Mich. We have been unable to locate a source of small-scale capsule machines, although Sharp and Dohme, Philadelphia 1, formerly supplied such a unit. Can one of our readers help Mr. Platt?—THE EDITOR

NO DOSAGE ON PRESCRIPTION DRUGS

Sirs:

Does the new labeling regulation require manufacturers to put dosage on the bottle? If not, it should. We pharmacists, under the law, are liable for an overdose; in case the physician prescribes an overdose we are to check with him, else the liability is ours. Sometimes the physician is not available, and these preparations that are flooding the market have on the label: Pamphlets will be mailed on request. Now we pharmacists are familiar with drugs that are used to compile prescriptions but it would take a public librarian to keep track of all the proprietary preparations now in use. . . .

Having the dosage on the bottle would help, and I know manufacturers would benefit. Physicians often come into my prescription room looking for something . . . that seems to fit the patient. Drugs labeled "write for pamphlet" are usually ignored. . .

Williamstown, Ky. J. B. MILLER

Sorry; dosage is not permitted on drugs bearing the prescription legend. This is intended to aid the pharmacist by making a clear-cut distinction between preparations with directions, which may be dispensed over the counter, and those with the legend, which must be restricted to prescription. Moreover, for many potent drugs the average dose in itself does not assure safe or proper administration. Authorities and physicians assume that the pharmacist will have full knowledge of the drugs he dispenses through professional training and study of professional journals and manufacturer's literature.—THE EDITOR

CARNOY'S MODIFIED SOLUTION

Sirs:

In the PRACTICAL PHARMACY EDITION recently I noticed a reference to Carnoy's Modified Solution. While working in an Army hospital I was asked to supply this solution and, after looking everywhere, a physician in Seattle sent me the following formula which may be of interest:

Absolute ethyl alcohol	6
Chloroform	3
Glacial acetic acid	1
Ferric chloride	1

Redondo Beach, Calif. AMOS M. PLANK

PHARMACY EMBLEMS FOR AUTOMOBILES

Sirs:

As a member of the A. PH. A., I wonder if you would locate for me the source of pharmacy emblems to be attached to the license plates of automobiles?. . . .It seems to me these were advertised at one time in your publications.

San Juan, P. R.

JESÚS D. DOMINGUEZ

Emblems of this type have been supplied by Bastian Brothers Co., Investment Bldg., Washington, D. C., but are available only in quantity for pharmaceutical groups.—THE EDITOR.

This department is your pharmacy forum. Do you have something to say on current affairs in the profession . . . a question to be answered? Write to the Journal at 2215 Constitution Ave., N. W., Washington 7, D. C.

STRAIGHT FROM HEADQUARTERS

by ROBERT P. FISCHELIS, Secretary
AMERICAN PHARMACEUTICAL ASSOCIATION

WE ARE rapidly approaching a show-down in the whole matter of veterans' employment, veterans' preference and the maintenance of adequate standards of service in the field of pharmacy. We have become accustomed to talking glibly about "taking care of the veteran" when he returns from military duty and presumably when we have been talking about taking care of him we have meant that he was to get his old job back, or that he was to be given preference for new jobs, or that he was to be given an opportunity to complete his education or to add to his education by graduate work or by some specialized training.

It can hardly be said that those who have been placing themselves on record as wanting to do something for the veteran have been giving lip service only, but it is undoubtedly true that many who have talked about veteran preference have done so without very much thinking or planning. Hence there will be occasions when individuals or concerns who have had every intention of looking after the interest of their veteran employees will find themselves in a somewhat difficult position because they have not planned properly, or perhaps had not expected the sudden influx of veterans brought about by the accelerated return of these men from their service posts.

Aptitude a Prime Essential

Our colleges of pharmacy, which have been complaining about the lack of students in the recent war years, suddenly find themselves overwhelmed in some instances, by large numbers of war veteran applicants to whom pharmacy was held out as a worth-while profession in the days preceding their separation from the Services. This situation requires considerable thoughtful planning, tactful administration, and sympathetic understanding.

In the first place, the pharmacy war veteran wants to come back to a profession which has gained rather than lost in prestige, in attractiveness, in better working schedules and emoluments and in opportunity for advancement.

The younger veteran who chooses pharmacy as his career without previous contact with the profession comes into it by way of the college of pharmacy. He has selected pharmacy because he has been told this profession offers unusual opportunities to the man or woman who aspires to a career of service to humanity as well as to a comfortable living.

The young men and women who have had several years of military service, now have the opportunity to obtain or complete a college education under very favorable conditions. As a matter of fact they can take chances on entering upon a college course, which they would ordinarily not attempt to do, because the government will pay their tuition and contribute toward their maintenance.

It is in the interest of the veteran, as well as in the interest of the profession and the public, which he will eventually serve, that high standards of practice as well as a high standard of admission be maintained, even though this may mean dropping some of these men and women from courses which they would like to pursue but which their scholastic record and aptitude tests definitely show they cannot pursue with profit.

It is neither a service to pharmacy nor to war veterans to load up a freshman class in a college of pharmacy with a group of students, who would ordinarily not qualify for admission to the pharmacy course, just because they are able to pay tuition and maintain themselves through government funds. If the colleges of pharmacy maintain established standards but fail to screen carefully all applicants for admission, they may find before the freshman year is over that a large percentage of veteran students may have to be dropped. Should this be the case, it would mean that considerable numbers of capable persons who are not veterans may have been denied the privilege of taking the pharmacy course and the profession itself may have been deprived of necessary capable personnel.

It is so much better to come to grips with this problem at the beginning and to employ the "ounce of prevention," rather than to complicate

the problem for the profession, the institution and the individual by promoting a false sense of service to the veteran.

The most important service we can render the veteran is to provide vocational guidance based upon established standards and a measurement of the aptitude and capability of the individual for the work he would like to do.

In pharmacy, as in other fields of endeavor, we are confronted with a lack of adequate data and information which would automatically provide guidance for all concerned. For example, there are very few states, if in fact there are any, which know definitely how many pharmacies are needed to provide the service that is essential for the civilian population. There is still a lack of information as to the number of pharmacists required to properly man existing pharmacies and supply personnel for other branches of the industry and profession. There is considerable lack of information on the degree of specialization that should be fostered in the undergraduate pharmacy course and the extent to which graduate instruction is needed or the direction which it ought to take.

All of this information was to be supplied by a series of surveys covering the industry and the profession, but these surveys have not yet materialized. They will not materialize until the profession and the industry, through one or more of their sources of financial aid, will inaugurate these surveys. Perhaps the most constructive proposal that has yet been made is that of the American Association of Colleges of Pharmacy which has endeavored to induce the American Foundation for Pharmaceutical Education to finance a general survey of pharmaceutical practice and pharmaceutical education. If such an over-all survey is ever to be made, now is the time to make it.

As a matter of fact it is already too late to benefit as completely as possible from such a survey unless it is divided into one phase covering immediate necessities, and a second phase covering long-range requirements. The entire profession and industry will be benefited if a survey covering basic information to meet immediate needs could be gotten under way at once. It is good news that the American Council on Education is willing to undertake such a survey and the Council of the AMERICAN PHARMACEUTICAL ASSOCIATION is in hearty accord with the proposal.

War veterans do not want to be coddled, neither do they want to be fooled or be imposed upon. They deserve every proper consideration and advantage which will help to make up for the time they had to take out of their normal lives to do their share of fighting the war at the battle fronts. However they do not ask, nor should they be granted any unfair advantage at the expense of jeopardizing quality of service and public safety. Any attempt to construe acts of Congress or of state legislatures contrary to the public interest under the guise of helping war veterans will be resented most by veterans themselves because they fought to preserve the American way of life, not to destroy it.

Civil Service Victory

THE passage of H.R. 4717 creating a Department of Medicine and Surgery in the Veterans Administration, with the proviso that appointments to the position of pharmacist shall be limited to those who hold the degree of bachelor of science in pharmacy or its equivalent and registration in one of the states or the District of Columbia, has caused the U. S. Civil Service Commission to cancel its recently announced examination for pharmacists. The cancellation became necessary because the Civil Service Commission had invited persons with no college training in pharmacy to apply for the examination, along with others who have had formal training.

It is gratifying to note this reversal of the previously announced policy of the Commission, since it is in line with the point of view we have tried to express and promote through these columns and in prolonged correspondence with the president of the Commission.

It is to be expected that action in favor of formal education as a prerequisite for pharmaceutical service in the government recorded by the Congress in this legislation constitutes notice to the U. S. Civil Service Commission that standards of admission to the practice of pharmacy in the government service must be on a level that is at least as high as the requirements for registration in 45 of the 48 states and the District of Columbia. The new requirements should not operate to prevent continuous employment or advancement of pharmacists now in the Civil Service who qualified on the basis of requirements previously in effect. Gen. Bradley, director of the Veterans Administration, and Gen. Hawley, who heads the Department of Medicine and Surgery, are to be congratulated on their successful campaign to reorganize medical services in the Veterans Administration and we appreciate especially their constructive attitude with respect to the development of pharmaceutical services on a high plane.

Iron Salts IN NUTRITIONAL ANEMIA

by MELVIN W. GREEN

CHAIRMAN, COMMITTEE ON PHARMACEUTICAL RECIPE BOOK

ALTHOUGH anemia is a pathology that has been recognized for centuries, it is only in comparatively recent years that an adequate segregation of types of anemias has been accomplished. A gradual change in conception of the physiology of blood formation and the availability of new diagnostic methods have brought about this classification.

Basically, the anemias fall into two categories, anemia associated with blood loss or increased blood destruction, and anemia due to defective blood formation. Nutritional anemia falls largely into this latter category where there is a deficiency of iron due to an inadequate quantity of iron in the diet, a failure to utilize properly iron which is present or loss of iron by excessive hemorrhage. This anemia is also referred to as hypochromic microcytic anemia. The term, *hypochromic*, refers to the fact that there is a deficiency of hemoglobin in the individual cells even though there may be a normal number of cells present. Only hypochromic anemias (not hyperchromic and normochromic) respond to iron therapy. *Microcytic* means that the cells are smaller than normal.

Hematologists have developed ways of expressing these factors which, while somewhat empirical, are useful. To determine the average volume of an erythrocyte, a hematocrit is used. This instrument packs the red blood cells by centrifugation, and the volume of the packed layer is read from the instrument. The mean (average) corpuscular volume is determined as follows:

$$\frac{\text{Volume of packed cells per 100 cc. of blood}}{\text{Erythrocytes in millions per c. mm.}} \times 10 = \text{Mean corpuscular volume in cubic microns}$$

The normal values for this volume are: 105 at birth, falling rapidly to a childhood level of 87 to 73; adults 82 to 92. Thus, if the volume is greater than normal, the patient is said to have *macrocytosis;* if the volume is smaller than normal, the condition is called *microcytosis*, while the normal range is often spoken of as *normocytosis*.

The mean corpuscular hemoglobin may be calculated by use of the following formula:

$$\frac{\text{Hemoglobin in Gm. per 100 cc.}}{\text{Erythrocytes in millions per c. mm.}} \times 10 = \text{Mean corpuscular hemoglobin in micromicrograms}$$

Less carefully standardized are the *volume index*, *color index* and *saturation index*. These indices compare the value found for the patient with the normal, but unfortunately too many different values for normals are used to permit easy interpretation of the results. These indices are as follows:

$$\text{Volume index} = \frac{\text{Mean corpuscular volume (patient)}}{\text{Mean corpuscular volume (normal)}}$$

$$\text{Color index} = \frac{\text{Per cent of normal hemoglobin concentration}}{\text{Per cent of normal erythrocyte count}}$$

$$\text{Saturation index} = \frac{\text{Mean corpuscular hemoglobin concentration (patient)}}{\text{Mean corpuscular hemoglobin concentration (normal)}}$$

Iron Requirements

Normal male adults would appear to need about 5 to 8 mg. of iron per day to keep in equilibrium. Women between the ages of puberty

and the menopause need about two to four times this quantity, Leverton and Roberts having shown a need for 16 to 17 mg. per day.

Although the average American diet contains from 10 to 20 mg. of iron, the failure to eat an adequate ferrigenous diet, absorption failures, pregnancy and other periods of stress contribute to a state of nutritional anemia. At such a time, the average diet is inadequate to increase hemoglobin formation, for to increase the hemoglobin level 1% requires 25 mg. of iron for its formation. Since absorption is often far from 100%, it is obviously advisable to supplement the diet with iron preparations during such periods.

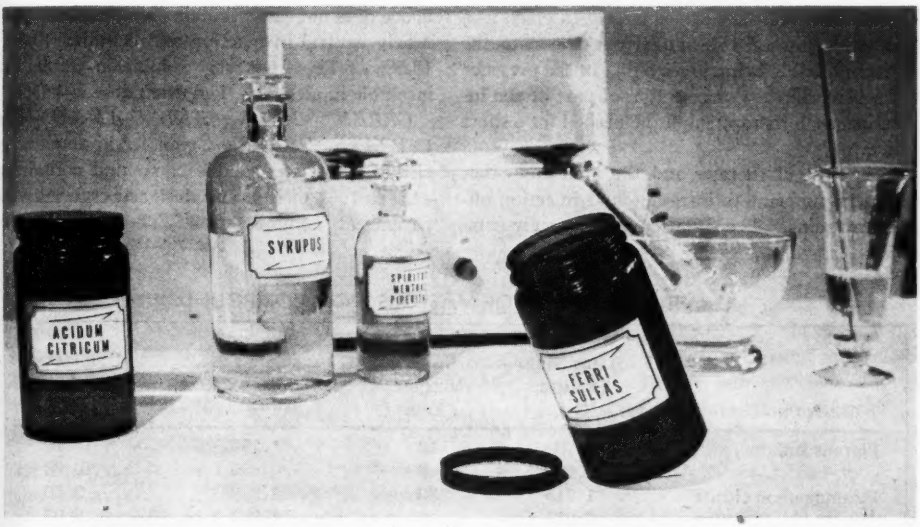
Types of Iron Compounds

Both organic and inorganic salts of iron are available for use in medicine. For many years a controversy has raged over whether the inorganic salts or the organic salts were most effective.

It was at first believed, with little evidence, that only the organic compounds and, in fact, only hemoglobin could be successfully absorbed and utilized in blood formation. Later, when it was unequivocally shown that inorganic compounds could be absorbed, attention was turned to the degree of absorption and utilization of organic *vs.* inorganic iron, and of ferrous *vs.* ferric iron.

So many factors influence iron absorption and utilization that these basic points are easily obscured. The tendency to use inadequate doses of iron and the failure to take into account the actual iron content of various compounds have also contributed to the confusion. Present evidence appears to indicate that all forms of iron, even the metal, are utilized to some extent, but that iron in a nonionic form and incapable of reacting with dipyridyl is poorly absorbed.

Hahn and co-workers have studied this problem by the very effective and dramatic means of administering radioactive isotopic iron, Fe^{59}. In these studies it was shown that ferrous iron was definitely better absorbed than the ferric, when such "tagged" iron was fed to humans. In dogs, made anemic by bleeding, the same thing was found. It was shown also, by these experiments, that the individual response to a given dose of "tagged" iron is so variable that one cannot study the relative utilization of different iron preparations in different subjects, a fallacy neglected in many previous studies.



FERROUS SULFATE SYRUP will be in N. F. VIII as a new prescription formula.

The use of "tagged" iron will no doubt modify many of our previous concepts regarding iron absorption, utilization and storage. Present conceptions, limited though they may be, indicate that iron is absorbed mainly in the duodenum and upper jejunum, and in progressively decreasing amounts in the remainder of the jejunum and the ileus. Probably no absorption takes place through the stomach, but the gastric

acidity contributes to making the iron soluble. A loss in acidity, if concomitant with a low iron intake, is detrimental to proper iron balance. The combined alkalinity, phosphate and protein content of the lower gut precludes absorption from this region.

Once the iron is absorbed, experience indicates that there is negligible excretion. The largest portion of the iron is in the erythrocytes as hemoglobin, but some nonhemoglobin iron exists in the erythrocytes also. In addition, some iron is found circulating in the plasma. About 7% of the body iron is present in the muscles as muscle-hemoglobin iron. Most of the remainder of the iron is stored in the viscera, especially in the liver and spleen.

Parenteral Administration of Iron

The intramuscular injection of iron is certainly the only permissible method of parenteral administration. Even this use is open to a great deal of question. Certainly no salt of iron capable of precipitating protein should be used. This would limit the choice largely to green iron and ammonium citrate and ferrous gluconate, the latter probably being preferred. In the presence of severe diarrhea or resection of part of the intestine, such therapy might be needed for a short time.

The cost of therapy and the pain and other dangers pursuant to intramuscular injection offset any gains. The situation is adequately summarized by Heath and Patek [*Med.*, 16:267, 1937], who state, "The authors have not as yet observed a single case in which iron given by injection succeeded in promoting blood formation when by mouth it failed to do so."

The following is a list of some of the important iron preparations and their properties:

REDUCED IRON, U. S. P.—Since reduced iron is iron in the metallic state, it obviously depends upon the hydrochloric acid of the stomach for its conversion into the soluble state. Consequently this form is inadequate in the presence of achlorhydria. In the presence of normal gastric acidity it appears to be absorbed as well as ferrous salts.

Obviously it can be dispensed in capsules, tablets and pills only. In moderately severe anemia, it is usually given in doses of 1 to 1.5 Gm. two or three times daily. After the patient's blood level has returned to normal, a maintenance dose of about half to a third of this amount is sufficient, if maintenance therapy is necessary.

IRON AND AMMONIUM CITRATE, U. S. P.—This ferric salt contains nonionic iron, and hence does not cause protein precipitation. It is nearly neutral in reaction and contains 16.5 to 18.5% of Fe. It is very soluble in water, but insoluble in alcohol. The usual dose is 1 Gm.

GREEN IRON AND AMMONIUM CITRATE, U. S. P.—Green ferric ammonium citrate is a water-soluble compound containing 14.5 to 16% of iron and designed especially for parenteral administration. The iron in this

RELATIVE EFFICIENCY OF VARIOUS IRON COMPOUNDS*

Compound Used	Daily Iron Dosage, Gm.	Number of Doses	Average Daily Hemoglobin Rise, %	Utilization of Iron, %
Ferrous sulfate	0.180	12	1.175	15.70
" "	0.120	3	0.650	13.00
Fe ammonium citrate	1.215	30	1.270	2.50
" " "	1.215	3	1.030	2.03
Ferrous carbonate	0.110	6	0.96	20.80
" "	0.110	3	0.520	11.30
" "	0.220	8	0.803	8.80
" "	0.220	1	0.180	1.96
" "	0.330	10	1.125	8.18
" "	0.330	3	0.940	6.84
Ferrous chloride	0.132–0.198	4	1.420	20.70
" "	0.132–0.198	3	1.000	14.50
Ferrous gluconate	0.108	1	1.550	37.50
" "	0.108	5	1.230	29.00
" "	0.216	2	1.240	17.25

* After Reznikoff and Goebel [*J. Clin. Invest.*, 16:547, 1937].

compound has about the same availability as that of the garnet-colored scales of iron and ammonium citrate.

The greatest disadvantage to its parenteral use is the pain associated with the injection site. It is given in doses of 60 mg., the maximum permissive dose being 100 mg.

FERROUS SULFATE, U. S. P.—Ferrous sulfate is freely soluble in water and insoluble in alcohol. It contains about 20% of Fe. While ferrous sulfate is utilized more efficiently than some of the ferric complexes, its ability to liberate sulfuric acid upon hydrolysis and to precipitate protein gives it undesirable, irritating qualities.

The National Formulary has admitted a formula into N. F. VIII for making Ferrous Sulfate Syrup. This formula is a modification of one originating with Donald A. Clarke, a prominent hospital pharmacist. It contains about 0.32 Gm. of ferrous sulfate per dose. The ingredients are readily available, and it can be made easily by the pharmacist:

FERROUS SULFATE SYRUP

Ferrous sulfate	40	Gm.
Citric acid	2.1	Gm.
Peppermint spirit	2	cc.
Sucrose	825	Gm.
Distilled water, *q. s.*		
To make	1000	cc.

Dissolve the ferrous sulfate, the citric acid, the peppermint spirit, and 200 Gm. of sucrose in 450 cc. of distilled water; and filter the solution until clear. Then dissolve the remainder of the sucrose in the clear filtrate, add sufficient distilled water to make 1000 cc., and, if necessary, strain through a pledget of cotton.

Average Dose—8 cc. (2 fluid drachms).

SACCHARATED FERROUS CARBONATE, N. F.—This compound is another source of inorganic iron. It has the disadvantage of the need for a very large dose, however. Modern therapy calls for the use of 2 to 4 Gm. of ferrous carbonate daily, and since this compound contains but 15% ferrous carbonate, the bulk becomes prohibitive.

*FERROUS GLUCONATE.**—Ferrous gluconate, introduced into medicine by Reznikoff and Goebel [*J. Pharm.*, 59:182, 1937, *J. Clin. Invest.*, 16:547, 1937], appears to be the most promising of the recently introduced National Formulary iron products. One of its chief advantages lies in its freedom from irritating properties. This is due to the fact that it does not precipitate proteins nor liberate strong acids by hydrolysis. It is very stable in the solid state, and its solutions are stable when sealed in ampuls. Its parenteral administration appears to be free from irritation. The table from Reznikoff and Goebel, on page 58, shows the comparative utilization of several iron compounds in humans. The variation of response in different individuals shows the need for using the individual as his own control.

It is of interest that these clinicians found that patients, who were irritated by ferrous sulfate, tolerated ferrous gluconate very well.

* Ferrous gluconate has been admitted to National Formulary VIII.

Unofficial Preparations

For those who desire to vary the source of iron from the usual official preparations, the following formulas taken from the *Pharmaceutical Recipe Book* may prove to be of interest:

SYRUP OF FERRIC HYPOPHOSPHITE

Ferric hypophosphite	17 Gm.
Potassium citrate	25 Gm.
Sucrose	850 Gm.
Orange flower water	90 cc.
Distilled water, a sufficient quantity	
To make	1000 cc.

Dissolve the ferric hypophosphite and the potassium citrate in 225 cc. of distilled water with the aid of heat, and filter. Mix the filtrate with the orange flower water, add sufficient distilled water to make the solution measure 450 cc. and dissolve the sucrose in this liquid with the aid of gentle heat. Finally add sufficient distilled water to make the product measure 1000 cc.

Average Dose—Metric, 4 cc.—Apothecaries, 1 fluid drachm.

COMPOUND SYRUP OF IRON PHOSPHATE

Soluble ferric phosphate	37.5	Gm.
Quinine sulfate	37.5	Gm.
Strychnine sulfate	0.5	Gm.
Diluted phosphoric acid	250	cc.
Syrup, a sufficient quantity		
To make	1000	cc.

Dissolve the soluble ferric phosphate, quinine sulfate and strychnine sulfate in the diluted phosphoric acid, then add sufficient syrup to make the product measure 1000 cc.

Average Dose—Metric, 4 cc.—Apothecaries, 1 fluid drachm.

SYRUP OF FERROUS CHLORIDE

Syrup of Protochloride of Iron

Solution of ferrous chloride, R.B.	50 cc.
Glycerin	125 cc.
Orange flower water	125 cc.
Syrup, a sufficient quantity	
To make	1000 cc.

Mix the solution of ferrous chloride with the glycerin and orange flower water, and add sufficient syrup to make the product measure 1000 cc.

Average Dose—Metric, 4 cc.—Apothecaries, 1 fluid drachm.

NOTE—This syrup should be freshly prepared.

IRON CITRATE MIXTURE

(Gray)

Iron and ammonium citrate	32 Gm.
Citric acid	5 Gm.
Tincture of lemon	8 cc.
Syrup	750 cc.
Distilled water, a sufficient quantity	
To make	1000 cc.

Triturate the citric acid with the iron and ammonium citrate and dissolve in about 200 cc. of distilled water. Add the tincture of lemon and syrup and sufficient distilled water to make the product measure 1000 cc. Set aside for twenty-four hours and filter if necessary.

Average Dose—Metric, 4 cc.—Apothecaries, 1 fluid drachm.

ELIXIR OF FERRIC PYROPHOSPHATE

Elixir of Pyrophosphate of Iron

Soluble ferric pyrophosphate	35 Gm.
Distilled water	60 cc.
Aromatic elixir, a sufficient quantity	
To make	1000 cc.

Dissolve the soluble ferric pyrophosphate in the distilled water, with the aid of heat; add sufficient aromatic elixir to make the product measure 1000 cc. and filter.

Average Dose—Metric, 4 cc.—Apothecaries, 1 fluid drachm.

NOTE—A color change occurs in the above elixir which does not affect its medicinal value.

COMPOUND IRON MIXTURE

Griffith's Mixture

Ferrous sulfate, in clear crystals	6 Gm.
Myrrh, in small pieces	18 Gm.
Sucrose	18 Gm.
Potassium carbonate	8 Gm.
Spirit of lavender	60 cc.
Water or rose water, a sufficient quantity	
To make	1000 cc.

Triturate the myrrh, sucrose and potassium carbonate in a mortar with 700 cc. of rose water, at first added very gradually, so that a uniform mixture results. Add the spirit of lavender, then the ferrous sulfate previously dissolved in about 50 cc. of rose water, and lastly sufficient rose water to make the final preparation measure 1000 cc.

Average Dose—Metric, 15 cc.—Apothecaries, 4 fluid drachms.

NOTE—This mixture should be freshly prepared.

SWEET TABLETS OF IRON

Saccharated ferrous carbonate	13 Gm.
Cacao sugar tablet base, R.B.	17.5 Gm.
To make	100 tablets

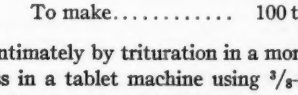
Mix intimately by trituration in a mortar, and compress in a tablet machine using $^3/_8$-inch die and punches, to make 100 tablets.

Average Dose—Child: 1 tablet.

Each tablet contains 0.13 Gm. (2 grains) of saccharated ferrous carbonate.

Not Simple Disease

No attempt has been made to discuss any form of anemia other than that due to simple iron deficiency. Anemia is not, however, a simple disease, but one which requires careful diagnosis by the physician and a treatment based upon the pathological findings. The pharmacist should acquaint himself with the limitations of the various hematinic agents on his shelves.



REMINGTON MEDAL PRESENTED

MEDALIST J. L. ROSIN (left) receives the award from Dr. Curt P. Wimmer.

AFTER a while the conversation turned to iodides and Prof. Remington said, "Joseph, Syrup of Iron Iodide bothers me. There is too much sugar in it, and in cold weather it crystallizes. Yet, if the quantity of the sugar is reduced, the syrup is unstable." Then, after a few moments of thinking, he said, "I think you and I should be able to do something about it." A short time later he died.

Thus Joseph L. Rosin, 1945 Remington Medalist, described his last visit with the great pharmacist to whom the Medal is dedicated. Since that time Mr. Rosin has done "something about" a great many chemical problems connected with the official compendia.

The importance of his service to American pharmacy was formally recognized at the testimonial dinner held December 11 in New York's Hotel Pennsylvania, when the Remington Medal was bestowed upon Mr. Rosin.

In his acceptance address, Mr. Rosin took issue with those who would have us believe that "the sun of pharmacy is setting . . . because the pharmacist no longer makes himself his extracts, tinctures, and so forth.

"No true science wanes or becomes extinct," he observed. Astrology, a pseudo-science, is gone and extinct, but not astronomy. A true science may take on new forms, it hews paths into new directions, but never ceases to blossom and bear fruit. It is ever fertile, ever multiplying and expanding.

"From pharmacy was born lusty, aggressive and fast-marching chemistry. The youngest of her offspring, pharmacology, has already won a seat of equality with the older members of the body scientific. Measured by Emerson's dictum that no science *is* a science unless it benefits mankind, pharmacy ranks high among the benefactors of humanity," he emphasized.

Speaking of the creative powers of science, Mr. Rosin predicted that the day may not be distant when knowledge will achieve for us almost complete independence of natural resources. "The younger generation may see the time," he continued, "when a nation's wealth will be measured not by the extent of her natural resources, but by the number of her scientists and research laboratories. The future of mankind rests with science."

Commenting on the misuse of scientific products, the Remington Medalist asked: Can we desist from speculating about the untold potentialities for a better world the atomic bomb holds, if we but temper its power with the engineering of the human heart.

In its own field, pharmacy, too, will meet the challenge of the future, he asserted. "In the changing scenes of the world the field for scientific pharmacy is rapidly expanding. The program for pharmaceutic education and training should be broadened to meet the new conditions."

Preceding Mr. Rosin's address, several pharmaceutical leaders, closely associated with the Medalist and his work, paid tribute to his achievements. These were Dr. George D. Beal, assistant director of the Mellon Institute of Industrial Research; Dr. E. Fullerton Cook, chairman of the U. S. P. Revision Committee; Dr. Justin L. Powers, chairman of the National Formulary Committee; Dr. Robert L. Swain, chairman of the U. S. P. Board of Trustees; and George W. Merck, president of Merck & Co. Presiding over the dinner meeting was Dr. Frederick D. Lascoff, president of the New York branch of the AMERICAN PHARMACEUTICAL ASSOCIATION.

CLINICAL TOXICITY OF THIOURACIL*

A SURVEY REPORTED TO THE
COUNCIL ON PHARMACY AND CHEMISTRY, AMERICAN MEDICAL ASSOCIATION
PREPARED BY

WALTON VAN WINKLE, JR., M.D.
Washington, D.C.

STANTON M. HARDY, M.D.
New York, New York

GEORGE R. HAZEL, M.D.
North Chicago, Illinois

DON CARLOS HINES, M.D.
Indianapolis, Indiana

H. SIDNEY NEWCOMER, M.D.
New York, New York

E. A. SHARP, M.D.
Detroit, Michigan

W. N. SISK, M.D.
Kalamazoo, Michigan

BECAUSE of the difficulty of determining from reports in the literature the incidence and severity of the toxic reactions resulting from the administration of thiouracil for the treatment of hyperthyroidism, a survey by questionnaire has been made of 5745 patients treated by 328 clinical investigators. The results derived from this survey have been analyzed by statistical methods and constitute the basis of this report.

Data obtained by questionnaire are subject to certain inherent errors. Failure to answer a question, misinterpretation of a question, and accidental insertion of an incorrect figure are among the sources of error in organizing such statistics. The necessity for arbitrary grouping and condensation of data and the inability to reflect secondary factors influencing the answer to a given question contribute to the errors of analysis. Some of these deviations can be held to a minimum by careful phrasing of the questionnaire and by intelligent interpretation of the answers. In a consideration of the data presented here, therefore, these inherent errors must be borne in mind although accepted statistical methods were used in their organization so as to limit the deviations to an irreducible minimum. It is believed nevertheless, that the trends disclosed and the conclusions reached as a result of this survey are correct, even though the statistics are subject to the errors mentioned.

Clinical Material and Therapeutic Appraisal

The material which forms the basis for this report is derived from large clinics, from small clinics, and from individual practitioners. Some of the patients were subjected to the closest scrutiny, which included repeated and extensive laboratory studies; others were followed in less detail.

Many patients were hospitalized, but many were ambulatory during treatment. Despite these variations, it is believed that the results of this survey represent closely those which may be expected when thiouracil becomes generally available to all physicians.

Since the clinical safety of any potent therapeutic agent should be appraised only in the perspective of its therapeutic usefulness, certain information regarding the value of thiouracil in the treatment of hyperthyroidism was collected. Published reports leave little doubt that in most instances the administration of thiouracil can bring about a remission of the hyperthyroid state. Its usefulness in other conditions associated with derangements of thyroid activity has not been completely evaluated.

This survey revealed that thiouracil is effective against all types of hyperthyroidism whether these be represented by diffuse or by nodular goitrés, and regardless of the number of nodules. Thiouracil may also be of value in the treatment of acute thyroiditis although data on this condition are scanty. The drug has been tried and found to be of no value in simple goitre. It has been tried without any useful effect in conditions with related symptomatology but where no hyperthyroidism exists.

An attempt was made to determine what, if any, factors contributed to a successful outcome of thiouracil therapy. The incidence of failure to respond to thiouracil has been correlated with such factors as dose, duration of treatment, and whether iodine therapy had been used prior to thiouracil. Only those cases in which thiouracil was used for treatment of hyperthyroidism are considered and failures directly attributable to toxic reactions are not included in the tabulations below.

A correlation could not be established between either the initial dose or maintenance dose and the incidence of failure. The number of cases receiving 0.1 Gm. per day as an initial dose is too small to be

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* From Drug Division, Food and Drug Administration, Federal Security Agency, and the Medical Departments of Lederle Laboratories, Abbott Laboratories, Eli Lilly and Co., E. R. Squibb and Sons, Parke Davis and Co., and the Upjohn Co. The authors wish to express their appreciation for the assistance of Miss Lila Knudsen and Mr. Pete James of the Food and Drug Administration, in the tabulation of the data and in their statistical analysis.

Reprinted from the *Journal of the American Medical Association*, February 9, 1946.

EDITOR'S NOTE: *Thiouracil, an important new drug for the treatment of all types of hyperthyroidism, has just been released for general use on prescription. Because of various reports on toxicity, FDA did not previously permit new drug applications to become effective until there was assurance that the value of the drug outweighed possible dangers of therapy. Maximum safety in the use of thiouracil will be achieved only through fully informed and constantly vigilant physicians and pharmacists. Since pharmacists share with physicians the responsibility of proper dosage, the* JOURNAL *considers the accompanying collaborative report to be of especial importance to its readers.*

Pharmacists may wish to distribute copies of the report to physicians, together with an announcement that the drug is in stock for prescription use. Reprints can be secured from THIS JOURNAL, *2215 Constitution Ave. N. W., Washington 7, D. C. Until March 10, up to five copies will be supplied without charge on request; additional copies are five cents each. Please enclose a large (No. 10) self-addressed stamped envelope.*

This report presents the latest and most authoritative information available on toxic reactions and dosage. For further information on the development of thiouracil, and its chemistry, properties and pharmacology, please see the earlier paper in THIS JOURNAL, *6:359, 1945 (December).*

statistically significant. The majority of investigators used either 0.4 Gm. per day or 0.6 Gm. per day, and since the results are as satisfactory at the lower figure as at the higher, it would appear preferable to recommend 0.4 Gm. per day as the initial dose.

Clinical experience has shown that thiouracil should be administered in divided doses throughout the 24-hour period. Administration only once a day is generally followed by poor results. For best results it is suggested that the total daily dose be divided into 3 or 4 parts which are administered at equal intervals during the waking hours.

It has been a common observation that a clinical response to thiouracil may not be seen for several weeks after treatment is started. In this survey there were 209 failures reported in which the duration of treatment was given. Figure 1 shows that the incidence of successful treatment increased as the duration of treatment was prolonged. No explanation is apparent for the low incidence of success at six months, but the figure for thirteen months was derived from too small a number of patients to be significant. To emphasize the desirability of prolonged treatment before classifying a lack of response as a failure, it was observed that in 34% of those patients reported as failures, treatment was discontinued before the eighth week.

It is not uncommon for a patient to show no response to thiouracil in the first four to eight weeks of treatment if iodine had previously been administered or if the gland was large and soft. It is noteworthy, therefore, that of the 71 failures which occurred during the first eight weeks, 70% had had iodine therapy prior to thiouracil treatment. This suggests that some might have responded satisfactorily if the medication had been continued for longer periods.

TABLE 1.—FAILURES OF THIOURACIL THERAPY IN RELATION TO INITIAL DOSE OF THIOURACIL

INITIAL DOSE, GM./DAY	TOTAL CASES	NO. OF FAILURES	PER CENT FAILURES
0.1	35	0	0
0.2	268	9	3.4
0.3	187	12	6.4
0.4	669	30	4.5
0.5–0.6	3448	135	3.9
0.7–0.9	504	32	6.3
1.0 or over	622	31	5.0
TOTAL	5733	249	4.3

FIG. 1—Relation of satisfactory response to thiouracil to duration of Treatment.

It was not possible to obtain reliable figures on the incidence of remissions induced by thiouracil. By remission is meant absence of symptoms and a basal metabolic rate within the normal range after the drug was discontinued. The majority of investigators did not terminate treatment except in those cases where thyroidectomy was performed, hence there is no way to determine the duration of remission without the drug. It is evident, however that of the 1236 remissions reported in this series 33.7% had relapsed at the time of inquiry. Remissions as long as a year or more have been reported, but the average relapse occurred in about twenty weeks. Hence, until more is known regarding the conditions influencing both remission and relapse, it is futile to speculate on this problem.

Type and Incidence of Toxic Reactions

The principle toxic reactions observed following medication with thiouracil are: granulocytopenia, leukopenia, drug fever, and dermatitis. At least 27

other reactions were recorded, of which only 8 were observed in more than 2 cases. This suggests that most of the reported side-reactions other than those specifically named or the eight mentioned later were not related to thiouracil medication.

Twenty-eight investigators reported that the drug occasionally produced nausea sometimes accompanied by dizziness, headache, or abdominal cramps. Parotitis and joint pains have each been reported by 7 investigators. Purpura was reported by 6, jaundice by 4, diarrhea by 4, thyroiditis by 3, and secondary anemia by 3 investigators. Edema, particularly of the extremities, has been mentioned by several investigators as occurring during therapy. It is not clear in all cases that this was due either directly to the drug or to the rapid metabolic and circulatory changes resulting from correction of the hyperthyroidism.

The eight complications of low incidence may or may not be related to administration of thiouracil, since these reactions did not occur with a frequency greater than expected in 5000 persons selected at random and observed for a period of six months to a year. It is recommended, however, that these complications should be watched for since it cannot definitely be proved that the drug was not the responsible agent.

In the series studied in this investigation, 752 cases in which one or more side-reactions occurred were reported. This represents an incidence of 13.1%. These complications were considered by the investigators as severe enough to warrant discontinuance of therapy of 452 patients or 60.1% of those showing some side-reaction.

Granulocytopenia

Since the most serious complication of thiouracil therapy appears to be granulocytopenia, it was pertinent to inquire concerning the frequency of this complication and whether its occurrence could be correlated with the dose, duration of treatment, or other factors. A diagnosis of granulocytopenia was accepted if the total white count was below 4000, the granulocytes markedly diminished, and associated with sudden onset and acute symptoms such as fever, sore throat, prostration, and malaise. Unfortunately not all cases of apparent malignant granulocytopenia are clearly distinguishable from simple neutropenia, particularly in the early stages.

The investigators reported one hundred and sixty eight case of granulocytopenia, but only 142 of these could clearly be classed as the frank malignant type. The remaining 26 cases appeared to be early cases or atypical simple leukopenia with neutropenia, but because the investigators classed them as granulocytopenia they are included as such in these tabulations. The 142 cases of granulocytopenia represent an incidence of 2.5% of this complication and accounted for about 22% of all toxic reactions.

It can be seen from Table 2 that there is no significant relationship between the incidence of granulocytopenia and dosage of thiouracil.

TABLE 2.—INCIDENCE OF GRANULOCYTOPENIA DURING THIOURACIL THERAPY IN RELATION TO INITIAL DOSE

Initial Dose Gm./Day	Total Cases	Granulocytopenia Cases	Per Cent of Total Cases
0.1–0.4	1159	33	2.8
0.5–0.6	3448	109	3.2
0.7–0.9	504	14	2.8
1.0 and over	612	12	2.0

There was, however, a very clear relationship between the duration of treatment and occurrence of this complication. Figure 2 shows that the incidence of granulocytopenia was greatest during the first four weeks of treatment and declined progressively thereafter. The incidence of this complication in the first month of treatment was 1.4% and more than one half of all the cases occurred during this period. Seventy per cent of the cases of granulocytopenia occurred by the end of the eighth week of treatment. No apparent explanation was found for the high incidence during the seventh month of treatment, but it is suggested that some patients may have lapsed in treatment at this time, and it is generally believed that resumption of therapy after such a lapse may predispose the patient to this complication.

One case of agranulocytosis was reported to have occurred during the fifty-sixth week of treatment, and 1 case, not included in these tabulations, was reported to have occurred six months after discontinuance of treatment. The first case may also have occurred after a temporary discontinuance of therapy.

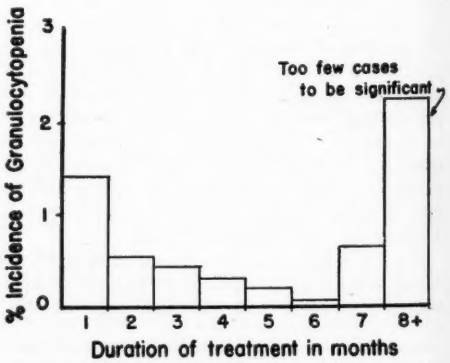


FIG. 2—Relation of incidence of granulocytopenia to duration of treatment.

There were 21 deaths, all attributable to agranulocytosis, establishing a mortality rate of 0.4% for the entire series and a case fatality rate for agranulocytosis of 14%. From the information available in the literature and that obtained in this survey, the most effective treatment of agranulocytosis appears to be the parenteral administration of massive

doses (500,000 units per day) of penicillin and some investigators suggest repeated transfusions of small amounts (200 to 300 cc.) of whole blood. However, there are some who are not in favor of unnecessarily frequent blood transfusions because it has been shown statistically that repeated transfusions increase the risk of transfusion reaction. There is no satisfactory evidence that pantothenic acid, pyridoxine, folic acid, vitamins, or pentnucleotide influence the outcome of this disease or aid in preventing such reactions.

The most important factor in the control of granulocytopenia resulting from thiouracil therapy appears to be discontinuance of therapy at the earliest sign of this complication and prompt institution of vigorous treatment. It is imperative that the patient be instructed to stop the drug and report immediately to the physician if symptoms such as sore throat, fever, coryza, or malaise are noted. The value of repeated blood counts is emphasized by the fact that one patient was found to have a complete absence of granulocytes three days before any symptoms developed.

Leukopenia

One third of all the reported toxic reactions consisted of a leukopenia. In many instances it was difficult to distinguish between a simple leukopenia and an early malignant granulocytopenia. In this survey a designation of simple leukopenia was made when the total white blood cell count was below 4000, the differential count was relatively normal, and the patient showed no subjective symptoms. It may be questioned whether all the cases of leukopenia reported were actually caused by thiouracil administration, since hyperthyroidism itself predisposes toward a leukopenic state. However, there seems to be a clear relationship between the administration of the drug and the onset of this complication and it is felt that any reduction in total white count while the patient is under treatment with thiouracil should be viewed seriously.

Of the 251 cases of leukopenia reported in this series, 234 lend themselves to fairly detailed analysis. This complication had an over-all incidence of 4.4%. From Table 3 it may be seen that dosage bore no relationship to the incidence of leukopenia.

TABLE 3.—INCIDENCE OF LEUKOPENIA IN RELATION TO INITIAL DOSE OF THIOURACIL

Initial Dose, Gm./Day	Total Cases	Leukopenia Cases	Per Cent Incidence
0.1–0.4	1159	58	5.0
0.5–0.6	3448	119	3.5
0.7–0.9	504	44	8.7
1.0 and over	622	30	4.8

The relationship between incidence and duration of treatment is shown in Fig. 3 and resembles closely that of granulocytopenia. The incidence of leukopenia in the first four weeks was 2.7%, and 60% of all these cases occurred during this period. Seventy-five per cent had occurred by the end of eight weeks and 95% by the end of six months.

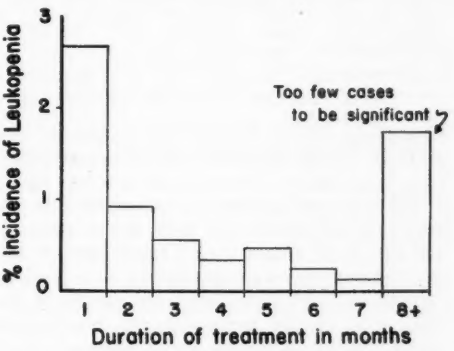


FIG. 3—Relation of leukopenia to duration of treatment.

In a number of cases in which leukopenia developed, administration of thiouracil was continued and in nearly half of these a gradual return of the white cell count to normal limits was observed. No reliable figures were obtained on the seriousness of this complication and it appears that in some instances it may not be harmful to the patients. However, since it cannot be predicted which case may or may not have a serious prognosis it would seem imperative either to discontinue treatment or have the patient report to the physician at frequent intervals for repeated examinations of the blood. Hospitalization of the patient should be considered if there is a decided reduction in granulocytes.

This precaution is further emphasized by the fact that although 121 patients developed granulocytopenia without a previous leukopenia, and 198 patients developed a leukopenia which did not pass into a granulocytopenia, 47 patients had both complications. If these two complications were to occur in the same individual purely on the basis of chance, it would be expected that these would occur in not more than 7 or 8 patients in a series of the size studied. The actual incidence was six and one-half times the expected incidence, and the difference, when tested by statistical methods, was found to be highly significant ($P. < .001$). This suggests that all patients who develop a leukopenia during therapy should be closely watched.

Drug Fever

Drug fever is a reaction not infrequently seen following therapy with a wide variety of substances. It is not surprising, therefore, that this complication was reported in 154 individuals following thiouracil therapy. The incidence of this reaction amounted to 2.7% of all cases and accounted for 20.5% of all toxic reactions. By reference to Table 4 it is evident

TABLE 4.—INCIDENCE OF DRUG FEVER IN RELATION TO INITIAL DOSE OF THIOURACIL

Initial Dose, Gm./Day	No. of Cases	Cases with Drug Fever	Per Cent Incidence
0.1–0.4	*1159	37	3.2
0.5–0.6	3448	86	2.5
0.7–0.9	504	10	2.0
1.0 and over	622	21	3.3

that dosage did not influence the incidence of this reaction. Furthermore, this reaction usually occurs early in the course of therapy as is shown in Fig. 4.

Thirty per cent of these reactions occurred in the first week of therapy and 85% had occurred by the end of the fourth week. Nearly 10% of the cases of drug fever were observed in the first forty-eight hours, and if the patient was retested with the drug, fever usually occurred in less than twelve hours. An interesting observation made by several investigators was that when drug fever occurred early in therapy it was usually a more severe reaction, with temperatures as high as 106° F. reported in some instances. In those instances in which the fever was seen during the later stages of therapy, the temperatures seldom exceeded 102° F., and the entire reaction was of a milder nature. Since a fever is part of the syndrome of agranulocytosis, any patient receiving thiouracil who develops a fever should be examined immediately and white blood cell and differential counts should be obtained in order to rule out agranulocytosis before classifying the fever as a temperature reaction only.

Skin Reactions

The skin reactions which occurred during thiouracil therapy were varied and usually of a mild nature. One hundred and eighty nine instances of these complications were observed, an incidence of 3.3%. One-fourth of the adverse reactions from thiouracil were skin reactions. The frequency of the various types of skin reaction is shown in Table 5. As might be expected, dosage had no influence on the incidence, and although there was some tendency for the reactions to occur early in treatment, particularly if other complications occurred in the same patient, the relationship between duration of treatment and incidence was not as striking as that seen with the other complications.

Although none of the skin reactions was reported as serious, the occurrence of urticaria cannot be regarded as an innocuous reaction. In the case of the sulfonamides such reactions have frequently been associated with more severe complications, hence it would seem advisable to discontinue thiouracil therapy or proceed with great caution if the patient shows an allergic response.

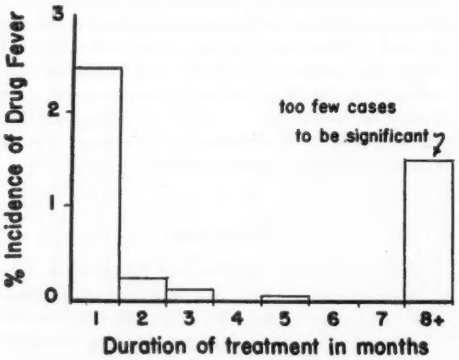


FIG. 4—Relation of drug fever to duration of treatment.

TABLE 5.—SKIN REACTIONS FROM THIOURACIL THERAPY IN 5745 PATIENTS

Urticaria	64 cases
Papular rash	37 "
Morbilliform rash	23 "
Erythema	18 "
Macular rash	17 "
Acneform rash	3 "
Pruritus	3 "
Edema of legs	1 "
Unspecified dermatitis	23 "

Opinion Survey

Because of relatively high incidence and severity of the toxic reactions following thiouracil therapy, an attempt was made to poll the investigators regarding their opinions of the relative safety of this drug.

The following question was asked:

> In your opinion is the incidence of toxic reactions greater than the incidence of bad results (including postoperative thyroid crisis, injury to recurrent laryngeal nerve, parathyroid tetany, and other operative complications; uncontrolled or fatal thyrotoxicosis in patients in whom operation is inadvisable or contraindicated) seen with other methods of treatment?

The answers to this question are summarized in Table 6. It is apparent that the large majority of those who have had experience with thiouracil feel that it offers a definite advantage over present

TABLE 6

Opinions on relative safety of thiouracil. Is the incidence of toxic reactions to thiouracil greater or less than complications of present methods of treating hyperthyroidism?

Answer	Per Cent of Investigators
Less	78.6
Greater	4.2
No opinion	17.2

methods of treatment of hyperthyroidism from the standpoint of safety.

Summary and Recommendations

On the basis of this survey covering the experience of 328 investigators on 5745 cases the following recommendations appear justified:

1. Thiouracil is effective in the management of thyrotoxicosis and possibly thyroiditis.

2. Thiouracil is of no value and should not be used in other derangements of thyroid activity or in conditions not associated with hyperthyroidism.

3. More information should be secured concerning the induction of remissions by thiouracil and the factors affecting the permanence of these remissions.

4. At present, the optimum dosage schedule appears to be 0.4 Gms. per day, in divided doses initially, and after the symptoms are controlled or the basal metabolic rate is within the normal range the dose should be reduced to 0.1 or 0.2 Gms. per day. More information is needed on the effectiveness of lower doses.

5. On the basis of the available information, it can be recommended that thiouracil be used for pre-operative treatment or in those patients in whom operation is contraindicated. The wisdom of depending upon thiouracil as a substitute for operative procedures can only be determined by following the results of investigations carried on for longer periods.

6. Many patients, particularly those who have received previous iodine therapy, do not respond immediately to thiouracil therapy, hence medication should be continued for at least thirty days, or, for a patient to whom iodine has been administered, for sixty to one hundred days, before concluding that no response to thiouracil is possible.

7. Approximately 13% of all cases can be expected to show some adverse reaction to thiouracil therapy.

8. The most frequent and severe complications of thiouracil therapy are granulocytopenia, leukopenia, drug fever, and dermatitis. The appearance of jaundice, purpura, and anemia have been reported and should be watched for, and if observed call for a careful evaluation of the clinical condition of the patient before thiouracil therapy is resumed.

9. Granulocytopenia occurs in about 2.5% of cases and is the most serious complication of thiouracil therapy. This reaction tends to occur in the early weeks of treatment and 80% of the cases were seen by the twelfth week of therapy. No relationship to the dose of thiouracil was apparent. Treatment of this complication should consist of massive doses of penicillin (500,000 units per day).

10. Leukopenia had an incidence of 4.4%, occurred early in treatment (75% occurring in the first eight weeks) but was not related to dosage. More information is needed on the relationship between leukopenia and granulocytopenia.

11. Drug fever had an incidence of 2.7%, occurred very early in treatment (85% occurring in the first four weeks) but was not related to dosage. Reactions occurring early tended to be more severe than those occurring late in treatment.

12. Skin reactions had an incidence of 3.3%. Urticaria was the most common, but a wide variety of other dermatoses were seen. None were deemed serious, but caution is advised in continuing therapy in the presence of these complications.

13. Three-fourths of the investigators were of the opinion that the incidence of adverse reactions of thiouracil was less than the incidence of complications from present methods of treatment.

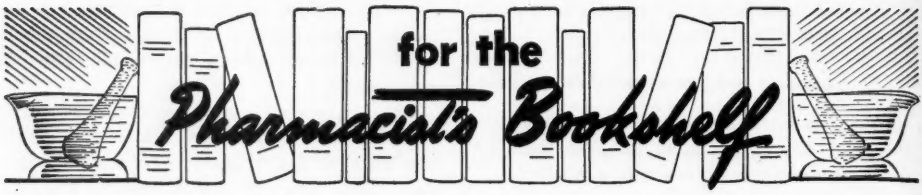
14. It should be emphasized that patients receiving thiouracil therapy should be carefully watched, especially during the first twelve weeks of therapy. Patients should be instructed to report immediately to their physician if any adverse symptoms such as sore throat, fever, coryza or malaise are experienced.

15. Since the mild and the juvenile types of hyperthyroidism can frequently be controlled adequately by iodine therapy alone, thiouracil should not be used for these patients unless the safer form of therapy proves ineffective.

SUBSTITUTING FOR TRADE-MARKED PRODUCT BRINGS LEGAL ACTION

Legal action has been instituted against retail pharmacists for substituting other mineral oil products when McKesson & Robbins' "Albolene" was called for. In announcing the action, McKesson & Robbins warned that it will continue to prosecute other retail pharmacists engaging in this practice to the full extent of the law.

Such substitute sales, the firm points out, violates property rights in the trade mark, undermines company good will and constitutes unfair competitive practice.



A WELL-BALANCED BASIC LIBRARY

GOOD reference books extend the pharmacist's professional horizon whatever his education may be. An up-to-date library, however small, is a sure mark of the progressive and successful pharmacy. Yet it is a department easily, and perhaps most often, neglected. In response to inquiries concerning a well-balanced reference shelf, THIS JOURNAL asked representatives of the AMERICAN PHARMACEUTICAL ASSOCIATION, American Society of Hospital Pharmacists and American College of Apothecaries to recommend their favorite volumes.

The basic list, given below, represents as nearly as possible the preferences of these successful pharmacists—the books they have found most useful and essential to modern practice. Representing a minimum goal, the primary list involves a total investment of about $80 for books which should have high priority on your purchases.

An additional investment of approximately $45 will be required for the supplemental list. Depending on the type of practice and special needs, some pharmacists may rightfully maintain that books in the supplemental group demand top priority. Since books, like friends, hold different values for different people, those surveyed may not have included one of your favorite volumes in this representative selection.

Primary List

1. PHARMACOPOEIA OF THE UNITED STATES XII (and Supplements)—*Mack Printing Co.*, 20th and Northampton Sts., Easton, Pa.; 380 pp., $7.50.
2. NATIONAL FORMULARY VII (and Supplements)—*Mack Printing Co.*, 20th and Northampton Sts., Easton, Pa.; 690 pp., $6.
3. UNITED STATES DISPENSATORY, 23rd Edition—H. C. Wood and Arthur Osol—*J. B. Lippincott Co.*, 227-231 S. 6th St., Philadelphia; 1881 pp., $15.
4. NEW AND NONOFFICIAL REMEDIES, 1945 (and Supplements)—*American Medical Association*, 535 N. Dearborn St., Chicago 10; 760 pp., $1.50.
5. PHARMACEUTICAL RECIPE BOOK III—*Mack Printing Co.*, 20th and Northampton Sts., Easton, Pa.; 551 pp., $5.
6. PRINCIPLES OF PHARMACY—H. V. Arny and R. P. Fischelis—*W. B. Saunders Co.*, W. Washington Square, Philadelphia; 1139 pp., $8.

   or

   REMINGTON'S PRACTICE OF PHARMACY (temporarily out of print).*
7. PHARMACOLOGICAL BASIS OF THERAPEUTICS—L. Goodman and A. Gilman—*Macmillan Co.*, 60 Fifth Ave., New York, N. Y.; 1387 pp., $12.50.

   or

   MANUAL OF PHARMACOLOGY, 6th Edition—T. Sollmann—*W. B. Saunders Co.*, W. Washington Square, Philadelphia; 1298 pp., $8.75.
8. MODERN DRUG ENCYCLOPEDIA AND THERAPEUTIC GUIDE, 2nd Edition—J. Gutman—*New Modern Drugs*, 49 W. 45th St., New York; 1644 pp., $10; NEW MODERN DRUGS QUARTERLY SUPPLEMENTS, $1 per year.
9. AMERICAN ILLUSTRATED MEDICAL DICTIONARY, 20th edition—W. A. Newman Dorland—*W. B. Saunders Co.*, W. Washington Square, Philadelphia; 1668 pp., $7.50.

   or

   GOULD'S MEDICAL DICTIONARY—*Blakiston and Sons*, 1012 Walnut St., Philadelphia; 1530 pp., $7.50.
10. MERCK MANUAL—*Merck and Co.*, Rahway, N. J.; 1836 pp., $2.
11. MERCK INDEX—*Merck and Co.*, Rahway, N. J.; 1060 pp., $3.
12. PHARMACEUTICAL CALCULATIONS—W. T. Bradley and C. B. Gustafson—*Lea & Febiger*, Washington Square, Philadelphia 6; 283 pp., $2.75.

    or

    COURSE IN PHARMACEUTICAL AND CHEMICAL ARITHMETIC—J. W. Sturmer—*Julius W. Sturmer*, 601 Lees Ave., Collingswood, N. J.; 147 pp., $2; ARITHMETIC OF PHARMACY—A. B. Stevens—*D. Van Nostrand Company*, 250 Fourth Ave., New York, N. Y.; 100

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* A useful volume in this general category, too new to have been evaluated by pharmacists, is AMERICAN PHARMACY—R. A. Lyman, Ed.—*J. B. Lippincott Co.*, E. Washington Square, Philadelphia 5; 540 pp., $8.

pp., $2 (or similar text in arithmetic).

Supplemental List

1. BACTERIOLOGY AND ALLIED SUBJECTS—Louis Gershenfeld—*Mack Publishing Co.*, 20th and Northampton Sts., Easton, Pa.; 561 pp., $6.
2. DRUG STORE ACCOUNTING—J. B. Heckert and W. E. Dickerson—*McGraw-Hill Book Co.*, 330 W. 42nd St., New York; 415 pp., $4.
3. DRUG STORE MANAGEMENT—H. C. Nolen and H. H. Maynard—*McGraw-Hill Book Co.*, 330 W. 42nd St., New York; 570 pp., $4.
4. SCOVILLE'S THE ART OF COMPOUNDING, 7th Edition—J. L. Powers and G. E. Crossen—*Blakiston Co.*, 1012 Walnut St., Philadelphia; 457 pp., $4.

   or

   PHARMACEUTICAL DISPENSING—W. J. Husa—*Husa Brothers*, College and Dubuque Sts., Iowa City, Ia., 428 pp., $4.
5. PHYSIOLOGICAL BASIS OF MEDICAL PRACTICE—C. H. Best and M. B. Taylor—*Williams & Wilkins Co.*, Mount Royal and Guilford Aves., Baltimore, Md.; 1942 pp., $10.
6. CHEMISTRY OF ORGANIC AND MEDICINAL PRODUCTS—G. L. Jenkins and W. H. Hartung—*John Wiley and Sons*, 440 Fourth Ave., New York; 675 pp., $6.50.
7. INCOMPATIBILITIES IN PRESCRIPTIONS—E. A. Ruddiman and A. B. Nichols—*John Wiley and Sons*, 440 Fourth Ave., New York; 337 pp., $2.75.
8. HANDBOOK OF CHEMISTRY—N. A. Lange—*Handbook Publs.*, Sandusky, O., 1750 pp., $6.

   or

   HANDBOOK OF CHEMISTRY AND PHYSICS—C. D. Hodgman, Ed.—*Chemical Rubber Publishing Co.*, 1900 W. 112th St., Cleveland, O.; 2221 pp., $3.50.

Other helpful books covering specific classes of preparations include the following:

CHEMISTRY AND MANUFACTURE OF COSMETICS—Maison G. De Navarre—*D. Van Nostrand Co.*, 250 Fourth Ave., New York; 745 pp., $8.

PENICILLIN AND OTHER ANTIBIOTIC AGENTS—W. E. Herrell—*W. B. Saunders Co.*, W. Washington Square, Philadelphia, Pa.; 348 pp., $5.

THE AVITAMINOSES, 2nd Ed.—W. H. Eddy and G. Dalldorf—*Williams & Wilkins Co.*, Mt. Royal and Guilford Aves., Baltimore, Md.; 519 pp., $4.50.

GLANDULAR PHYSIOLOGY AND THERAPY, 2nd Ed.—*American Medical Association*, 535 N. Dearborn St., Chicago; 570 pp., $2.50.

HANDBOOK OF OCULAR THERAPEUTICS, 2nd Ed.—S. R. Gifford—*Lea & Febiger*, 600 S. Washington Square, Philadelphia; 341 pp., $3.75.

DERMATOLOGIC THERAPY IN GENERAL PRACTICE—M. B. Sulzberger and J. Wolf—*Yearbook Publishers*, 304 S. Dearborn St., Chicago; 632 pp., $5.

PLANNING AND DESIGN SERVICE FOR PHARMACIES ESTABLISHED

A planning and design service for pharmacists who wish to remodel or open new pharmacies has been established by J. W. Snowden of Aurora, Ill. In addition to his new undertaking, Mr. Snowden will continue to serve the Pictorial Paper Package Corp. as product design and professional promotion consultant.

The new service will adapt structural design to the pharmacist's individual objectives, policies, competitive conditions and location.

After visiting 3000 pharmacies in 47 states, Mr. Snowden concluded that general plans supplied by mail would not prove satisfactory and therefore established an individualized service.

FDA ANNOUNCES PROMOTIONS

Appointment of Charles W. Crawford, present Assistant Commissioner of Food and Drugs, to the position of Associate Commissioner and the promotion of Dr. Louis D. Elliott and George P. Larrick to positions as Assistant Commissioners has been announced by Commissioner Paul B. Dunbar of the Food and Drug Administration.

Mr. Crawford is responsible for initiation of regulations and standards to be promulgated, in addition to serving as second ranking officer in the FDA. Dr. Elliott is responsible for law-enforcement operations related to foods and is in charge of import control work. Mr. Larrick will continue to have general charge of the inspection work of the field force and will also be responsible for law-enforcement operations relating to drugs and cosmetics.

The title of the FDA Drug Division has been changed to Medical Division to indicate more clearly the scope of its functions. Dr. R. P. Herwick, formerly holding the title of Division chief, has been given the title of Medical Director.

BOOK SERVICE

THIS JOURNAL will be pleased to obtain any professional book or periodical in print for its readers. Publications will be sent postpaid on receipt of check or money order covering the regular retail price. Address the Journal of the American Pharmaceutical Association, Book Dept., 2215 Constitution Ave., Washington 7.

U. S. P. XIII AND N. F. VIII INTRODUCE NE

by C. O. LEE

CON: The pharmacists of the country will soon know that their newly revised official standards, forthcoming in the United States Pharmacopœia XIII and the National Formulary VIII, have been Anglicized and greatly modernized. This has been done in an effort to make the books more useful to the physicians, the chemists, the enforcement officials, and the pharmacologists. The pharmacists are the forgotten men.

Pharmacists for these many decades have prided themselves upon their knowledge of Latinized titles for official drugs, chemicals and preparations. This was their stock in trade. In the future they will need to know only what other people know concerning the names of substances.

The vote of the Revision Committees to make English the language of the first title in the U. S. P. XIII and N. F. VIII came after no little discussion concerning the change. To some of us it seems that this change had to come. Latin has been abandoned by other pharmacopoeias, so it is quite natural that we in America should follow suit. It is unfortunate that all pharmacists could not be given a chance to vote upon this question, but such problems are decided by the Committees of Revision.

Titles in the U. S. P. XIII and N. F. VIII will be arranged in a strict alphabetic fashion according to English. It is further planned to arrange basic substances and their preparations together. For example, *Fluidextract of Belladonna* will not be found among the fluidextracts. It will be listed as *Belladonna Leaf Fluidextract.* This not only removes it from the customary grouping of fluidextracts, but changes the reading of the title which is new and strange to say the least. So it is with many other well-known products such as Aromatic Ammonia Spirit, Citric Acid Syrup, Glycyrrhiza Extract, and Lemon Tincture. We are used to this idea for chemicals and other simples but not for the other forms of administration.

Camphor Water will be found alphabetically under *C*, while Peppermint Water will be under *P*. Therefore, pharmacists must expect to find the traditional arrangement of preparations, so well known to them, completely erased from pages of

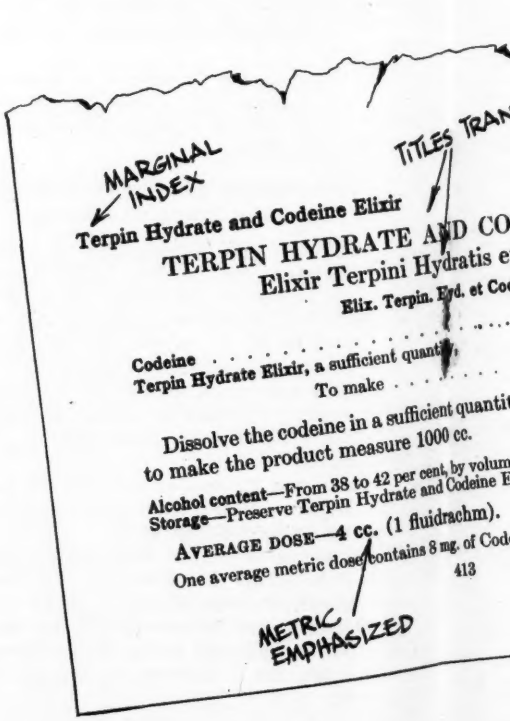
(*See Lee, page 72*)

EDITOR'S NOTE: Transposition of Latin and English titles in the new U. S. P. and N. F. has brought about a new plan of monograph arrangement. This break with tradition naturally raises several points for discussion. The JOURNAL *herewith publishes the views of Dr. C. O. Lee, of the Purdue University School of Pharmacy, who considers the new monograph arrangement, and the manner in which it was adopted, to be unsatisfactory. A letter by Dr. E. Fullerton Cook, chairman of the U. S. P. Revision Committee, is published on the facing page so that pharmacists may have both viewpoints on this question.*

The principal changes involved in the new arrangement are:

(1) The position of Latin and English titles will be reversed, but Latin will not be omitted.

(2) Each basic drug will be followed by monographs for its preparations. Instead of all tinctures being grouped together, for example, each one will follow the monograph for its principal active constituent. The titles *of all*


MARGINAL INDEX
TITLES TRAN
Terpin Hydrate and Codeine Elixir
TERPIN HYDRATE AND CO
Elixir Terpini Hydratis e
Elix. Terpin. Hyd. et Co
Codeine
Terpin Hydrate Elixir, a sufficient quanti
To make
Dissolve the codeine in a sufficient quantit
to make the product measure 1000 cc.
Alcohol content—From 38 to 42 per cent, by volum
Storage—Preserve Terpin Hydrate and Codeine E
AVERAGE DOSE—4 cc. (1 fluidrachm).
One average metric dose contains 8 mg. of Cod
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METRIC EMPHASIZED

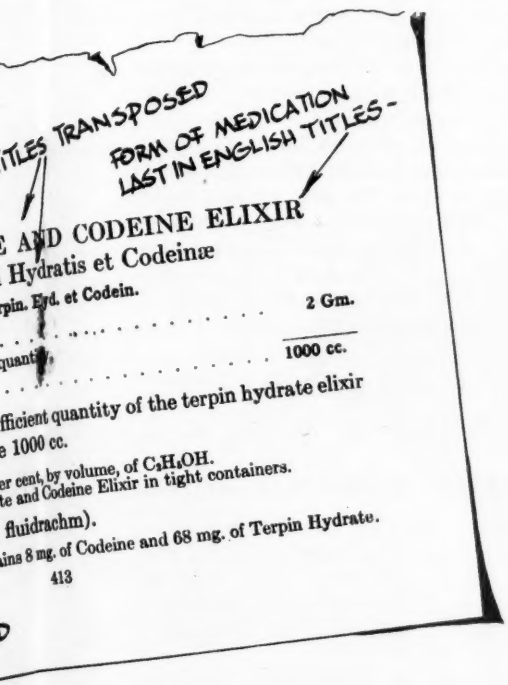
CE NEW ARRANGEMENT OF MONOGRAPHS

by E. FULLERTON COOK

tinctures will be grouped together under "T," however, with page references to the monographs.

(3) English titles will be reworded, where necessary, to bring about uniformity. In the present compendia, English titles appear in two ways: with the form of medication first (e.g., Tablets of Acetanilid); and with the form last (e.g., Chrysarobin Ointment). On this basis, Tablets of Acetanilid will be changed to Acetanilid Tablets.

(4) To overcome the complication of modifying words in certain titles (e.g., "Compound"), a marginal index of titles will be included as illustrated below. For example, Compound Pepsin Elixir will be an official title. Such an exception, will be listed in the marginal index as "Pepsin Elixir, Compound," so that the preparation will alphabetically follow the monograph for Pepsin, and thus preserve uniformity in the new arrangement. A cross reference will also be listed under "C" as a further measure to avoid any early difficulty in locating such monographs.


TLES TRANSPOSED
FORM OF MEDICATION
LAST IN ENGLISH TITLES -
E AND CODEINE ELIXIR
Hydratis et Codeinæ
rpin. Hyd. et Codein.
2 Gm.
1000 cc.
fficient quantity of the terpin hydrate elixir
e 1000 cc.
er cent. by volume, of C2H5OH.
te and Codeine Elixir in tight containers.
fluidrachm).
ains 8 mg. of Codeine and 68 mg. of Terpin Hydrate.
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DEAR DOCTOR LEE:

PRO: I was greatly surprised and much distressed to learn through your correspondence with Dr. Powers, as recently released in the National Formulary Circular, pages 1866 to 1874, that you felt that I had not given the members of the U. S. P. Revision Committee an opportunity to express their views or ask for a vote on the arrangement of monographs in the new Pharmacopœia.

The proposal, for title arrangement, was worked out in conference between Dr. Powers of the National Formulary Committee, Dr. DuMez, chairman of the U. S. P. Nomenclature Subcommittee, and myself, fully explained to the members of the Revision Committee, and to avoid any misunderstanding and to follow a thoroughly established program of Pharmacopœial revision the proposal was accompanied by a printed section clearly showing exactly how the plan would be applied if used in the new Pharmacopœia. I also presented the plan and showed the printed examples to many individuals, including prominent pharmacists and physicians and also to every group before whom I spoke during that period, and your letter of disapproval is the only opposition I have heard.

I assumed that your two letters to me were of the nature of personal correspondence for you never offered a motion to retain the previous Pharmacopœial order of arrangement which was always your privilege and the established rule of the Revision Committee. This would have at once opened the question for debate and a vote in the Committee.

I must say that I had hoped that the more extensive presentation of texts in the proof, following the proposed arrangement, had convinced you of the merits of the plan. Many others have expressed their complete approval and believe that it will increase the usefulness of the Pharmacopœia as a cooperative link between the pharmacist and the physician.

It should be of great help to the pharmacist, in extending information to physicians about Pharmacopœial medicines, to be able to open the Pharmacopœia and show his doctor friends page after page of standardized cardiovascular drugs, starting with the crude Digitalis Leaf, then the

(*See Cook, page 72*)

LEE (continued from page 70)

the U. S. P. and N. F. Elixirs, tinctures, waters, ointments, solutions, and the like will be scattered from A to Z throughout the books. In the official sense of the word the present classification of pharmaceuticals is doomed. This is a professional travesty which has been thrust upon the pharmacists of America through no choice of their own. What is even more ridiculous, the U. S. P. Committee of Revision has not had, up to this moment, the opportunity of accepting or rejecting, *by vote*, this new radical and questionable arrangement of monographs. We must not forget that when we destroy the traditional system of classification of pharmaceuticals we destroy one of the foundations upon which the profession has been built.

This radical new arrangement is most certainly more than an editorial prerogative. You may well ask, how did it all come about? This editorial is being written in an effort to find out. It will help greatly if you will join me in this inquiry.

. The proposed new arrangement of monographs of the forthcoming Pharmacopœia and National Formulary have appeared in the galley proofs of these two books. Whatever merits such an arrangement may have are in truth nullified by the fact that we, the pharmacists, are being forced to accept it without having any voice in choosing it.

Whose books are these? Are they for the doctors and the chemists, or are they for the pharmacists? Let us not forget that in 1906 the *pharmacists* furnished the government with legal standards useful in the enforcement of the then new Federal Food and Drugs Act. This is a fact of which pharmacy has a right to be proud.

Let's render unto Caesar what is Caesar's, but no more.

COOK (continued from page 71)

pharmaceuticals including a standardized Powdered Digitalis Leaf, Digitalis Capsules, Digitalis Tablets, Digitalis Injection, and Digitalis Tincture. Also Digitalin with its preparations, a Tablet and an Injection, and Digoxin with its Tablet and Injection, etc.

By the old arrangement this impressive evidence of up-to-date Pharmacopœial medicines, belonging to a specific class, would have been impossible.

So far as I can see the only advantage of the old arrangement whereby all Tinctures, all Tablets, all Ointments, etc., followed each other in alphabetical order, was for the teacher who wished to present an entire class of galenical products to his pupils when he discussed the characteristics of the class. Any one who wishes to do this will still find alphabetically in the new Pharmacopœia, under each class name, such as Tinctures, Tablets, Ointments, etc., a list of all U. S. P. representatives, with page numbers where the detailed monographs can be found. This was shown in the printed model. When this phase of the situation was discussed in my office it was believed that your views were fully covered by this feature of the plan.

I am particularly disturbed that you should feel that this or any other action of mine as Chairman of the U. S. P. Committee of Revision suggested a tricky or pressure administration. I have always endeavored to practice the utmost fairness in all relations and have complete confidence in the policy of open discussions and then the vote. Of course you know that it is impossible to vote on every U. S. P. proposal. We would have thousands of votes and for the large Committee to vote on every point would force many members to vote on matters in which they had no specific information. The policy, therefore, for years has been to accept many proposals without vote but always with the privilege given any member to move a reconsideration, to be followed by general discussion and a vote.

I wish that you had expressed yourself freely about this when you were with me in the Ointment Conference in Philadelphia on June 27th last. If you had done so I am sure we could have avoided any misunderstanding.

It is too late, of course, at this stage of the revision to alter the plan since it is already set up in the proof, but I hope that after you have used it for a while you will like it as much as the many who have already expressed their approval to me. As a teacher of pharmacy and as a pharmacist I can see no disadvantage, but many advantages to pharmacy through the change.

Sincerely yours,

E. FULLERTON COOK

PHARMACIST IS BUFFALO MAYOR

Pharmacist Bernard J. Dowd has been elected mayor of Buffalo, N. Y. After twenty-five years in the profession, Mr. Dowd will sell his prescription shop to devote full time to his executive duties. He is a graduate of the University of Buffalo.

The city's first mayor was also a pharmacist, according to the *Buffalo News*.

A NOTE ON
WRITING PRESCRIPTION LABELS

by ARTHUR A. HOEHN

FELLOW, AMERICAN COLLEGE OF APOTHECARIES
EAU CLAIRE, WISCONSIN

INTERPRET PHYSICIAN'S WISHES IN LANGUAGE THAT IS CLEAR, COMPLETE AND GRAMMATICAL

THE importance of intelligent interpretation of the "Sig:" on prescriptions filled by the pharmacist cannot be overemphasized. Too many pharmacists pass over the opportunity to tell the patient in adequate terms how to use the prescription which they so carefully, accurately and scientifically compound. It seems to me that an outstanding accomplishment that ought to be attained by any pharmacy and be particularly identified with all accredited pharmacies of the American College of Apothecaries is the writing of prescription labels "true to form," clear and complete.

The writer once served an apprenticeship under a pharmacist whose contention, in the form of a "must," was that the physician's "Sig:" must never, under any circumstances, be altered in the slightest—it must be transferred to the label just as it was written. Any violation of this practice was, in his estimation, the most serious offense that could be committed in the sanctum of his prescription room. While it is true that directions in those days were a bit more explicit than they are today, it still is true that his patrons often took home with them, on the labels of his carefully compounded prescriptions, an unintelligible assortment of directions. Too often it was necessary for some to call back for clarification of those same unedited directions. This, however, meant to him only a lack of intelligence on the part of the patron.

Then came a term of apprenticeship with a pharmacist who believed that it was the duty of the pharmacist to interpret the physician's instructions for the patient and to make the label intelligible. His "must" consisted of fully directing the manner of administration of the prescription. Sometimes he went so far as to write his interpretation on a sheet of paper. He made certain that no one had to return to learn what was intended. Many times patients commented on the thoroughness with which Mr. Jones saw to it that the directions were definitely understood. People liked being made to feel that the proper application of the medicine was important. His physicians liked it so well that they directed their patients to "take the prescription to Mr. Jones," because "he writes directions so you can understand them."

It is unfortunate that many pharmacists pursue the course of indifference by writing prescription directions with as few words as possible. Nothing looks more incomplete than a label with "As directed" on it. Just a few simple words will do much to make it appear complete. In this case, "Use as directed" —"Take as directed" —"Apply as directed," etc.

"One as directed" can be enhanced by "Take one tablet as directed"—"Take one capsule as directed." "Insert as directed" can be made more specific as "Insert into the rectum or vagina as directed." "Drop in eye at night" might be made to read: "Put one (1) drop into the eye at night." "Four drops in ear 3 times daily" would sound more complete if written: "Put four (4) drops into the right ear, three (3) times daily."

"One tab in glass water 3 times daily after meals" should read: "Dissolve one (1) tablet in a glass of water and take three (3) times daily,

From the *Bulletin of the American College of Apothecaries*, No. 7, 1945.

after meals," as was intended for the effervescent tablet prescription bearing the foregoing directions.

Then there is the case of Dr. Smith who writes: "℥i q. h. 2-3-4 as needed by cough." This should be directed "for cough," since medication is intended *for* a condition and not *by* a condition.

To many patients the "shake well" label on the bottle is not taken too seriously. To make the *shake* more important, it is a good idea to prefix the directions with: "Shake well and take" or "Shake well and apply," etc.

Instead of writing "to ear"—"to eye"—"on hand"—"on area," why not insert *the:* "To the ear"—"to the eye," etc., which make it sound less like a telegram?

When writing the frequently used "as needed" or "as required" why not "Use as needed" or "Use as is required"?

For directions on an insoluble powder intended to be taken in a liquid it is well to say: "Stir one (1) teaspoonful in a half glass of water and drink before it settles," instead of "One teaspoonful in liquid," etc.

I have before me a label from a drugstore which advertises: "Our pharmacists are specialists in prescription compounding." That may be true, but the advertisement neglects to mention that they write very poor direction labels. This label reads: "1-3 times daily until bowels get loose then 1 a day." Another: "One morning and Evening."

Here is one from an external prescription which might well be taken internally. There is no "external" label on the bottle and the directions read: "One teaspoonful in glass water 30 minutes every 4 hours during day." One teaspoonful of Burow's solution was to be added to a glass of water and the solution used to moisten the dressing, which was to be applied for thirty (30) minutes, every four (4) hours, during the day.

The following example is particularly bad for any kind of pharmacy: "2 after breakfast for 3 days increase 2-3 times a day first month then reduce to 1 or 2 a day." The entire puff in one breath, without punctuation! What was really intended for the patient's guidance was: *First three (3) days:* Take two (2) tablets after breakfast. *Next twenty-seven (27) days:* Take two (2) tablets three (3) times daily. *After that: reduce the dose to* one (1) tablet once or twice daily.

We would write the italicized words in red ink.

Many other instances could be cited of ways to assure that the physician's wishes are interpreted on the prescription label clearly, completely and in language always intelligible to the patient. Pharmacies accredited by the American College of Apothecaries should be meticulous in their attention to such details and lead the field in the art of writing better directions.

DRUG TRADE CONFERENCE MEETS

TEN resolutions, printed in full below, summarize the actions taken by the National Drug Trade Conference at its December meeting in Washington, D. C., the first session held since 1941. Nine member associations, including the A. PH. A., participate in the Conference, which is representative of all branches of the pharmaceutical profession and industry.

1

RESOLVED that the United States *Civil Service Commission** be requested to include pharmacists on the list of positions for which formal education is prescribed, and that a successfully completed full curriculum of study leading to a bachelor's degree in pharmacy in a college or university of recognized standing be made the minimum requirement for admission to the pharmacist examination for government positions.

2

RESOLVED that the National Drug Trade Conference recommends:

(1) That a complete *Census of Business*, as well as a complete *Census of Manufactures*, be made during 1947 covering the year 1946.

(2) That a complete Census of Business be made at five-year intervals thereafter concurrently with a complete Census of Manufactures covering the same calendar years.

(3) That the complete Census of Manufactures be taken quinquenially in place of biennially only if annual sample surveys providing adequate information with respect to sales by major product classifications can be undertaken.

(4) That annual sample surveys be made of at least the major retail and wholesale trades.

(5) That monthly reports based on selected samples be made of at least the major wholesale and retail trades, with wholesale data to be reported by geographical regions and retail data by states.

(6) That a copy of these recommendations be submitted to the appropriate officers of the Depart-

* Italics in resolutions have no significance except to simplify future reference to the stand of the Conference on specific subjects.

ment of Commerce and tc the Executive Secretary of each constituent member of the Conference.

3

RESOLVED that the National Drug Trade Conference favors enactment of the necessary legislation to *restrict administrative practice* wherein the administrative agency serves as prosecutor, judge and jury and to provide for impartial, speedy and capable independent determination of all disputed situations of fact.

4

RESOLVED that a committee composed of representatives of the members of the National Drug Trade Conference is hereby authorized to consider and report to the Conference on the feasibility of formulating *uniform legislation* of interest to the drug industry as a whole, the committee to consist of one delegate appointed by each conference member.

5

Whereas the *American Foundation for Pharmaceutical Education* is now firmly established and functioning in a very effective way toward development and promotion of pharmaceutical education, and

Whereas the National Drug Trade Conference unanimously sponsored the organization of the American Foundation for Pharmaceutical Education after many years of study by its Committee on Endowment and by the full membership in annual meetings of the Conference, and

Whereas all of the members of the National Drug Trade Conference are members of the American Foundation for Pharmaceutical Education, and

Whereas a large number in the drug industry have not as yet become patrons of the Foundation, now therefore be it

RESOLVED that the National Drug Trade Conference fully endorse the work of the American Foundation for Pharmaceutical Education and urge all members to give full support to its work and activities.

6

RESOLVED that the National Drug Trade Conference commends the efforts of the schools and colleges of pharmacy to improve and strengthen pharmaceutical education and urges the development of programs for *graduate study* which will yield the teachers needed to maintain the highest standards of education and the scientific personnel required by the industry for research and greater contributions to the public health.

7

RESOLVED that the National Drug Trade Conference record its approval of Senate 1417 introduced by Senator Saltenstall of Massachusetts which will give to the District of Columbia a *Fair Trade Act* similar to those now in effect in 45 states of the Union.

8

Whereas progress in the medical sciences and the rapid advancement in the production of drugs and pharmceutical preparations of a highly scientific character require greater foundational training as a basis for the professional courses in pharmacy, and

Whereas future practitioners of pharmacy will be called upon to a greater extent than ever before to supply information on these highly scientific products, be it

RESOLVED that the National Drug Trade Conference take every necessary step to safeguard the higher educational program for the training of pharmacists which has been developed in the past decade. To accomplish this end, be it further

RESOLVED that the National Drug Trade Conference urge that every effort be made to prevent the enactment of legislation which seeks to break down established *standards of pharmaceutical education and licensure* and, be it further

RESOLVED that the Conference re-affirms its belief that graduation from an accredited college of pharmacy with a four-year course of instruction is an absolute minimum qualification for admission to the practice of pharmacy, and be it further

RESOLVED that any effort to reduce the foregoing minimum requirement is deemed by this Conference to be contrary to the public interest, and be it further

RESOLVED that the recognition of any course in pharmacy which is not accredited by the American Council on Pharmaceutical Education is contrary to the best interests of students desiring to qualify for licensure as pharmacists and contrary to the best interests of the public, and be it further

RESOLVED that in order that *G. I. pharmacy students* gain the fullest advantage from their pharmaceutical education, they be urged to enroll only in schools or colleges of pharmacy accredited by the American Council for Pharmaceutical Education and in their own interest to refrain from undertaking any pharmacy courses at schools of pharmacy which are not so accredited.

9

Whereas the National Drug Trade Conference endorsed the proposal to place a *Pharmacy Corps* in the United States Army and was gratified when the Congress passed the necessary act which became Public Law 130, July 12, 1943, and

Whereas little progress has been made toward making this law effective, be it

RESOLVED that the National Drug Trade Conference calls upon the Surgeon General of the Army to take the necessary measures to activate this Corps as soon as possible.

10

Whereas it is becoming increasingly evident that the problems of pharmacy and the drug industry both commercial and professional may best be solved through *scientific research*, therefore be it

RESOLVED that the National Drug Trade Conference urges that all organizations within the drug industry give consideration to the support of scientific research projects for the solution of such problems and to the underwriting of fellowships for graduate work on such subjects.

Mystery of the FIRST ENGLISH PHARMACOPOEIA

by GEORGE URDANG

DIRECTOR, AMERICAN INSTITUTE OF THE HISTORY OF PHARMACY

IT WAS in 1585, three years before the Spanish Armada was defeated by the British, that the Royal College of Physicians of London considered for the first time "the compilation of a certain, public and uniform Pharmacopœia to be adopted by all apothecaries in this country."[1]

In spite of a definite decision on the groups of remedial agents to be dealt with in the proposed Pharmacopœia and the assignment of the special "classes" to those physicians who were regarded as experts in the fields concerned, no practical results were achieved.

The Annals of the Royal College of Physicians of London, in December 1594, reported a change in the commission for "the examination of our dispensatory." Then for twenty years silence prevailed. It was not until the twenty-fifth of June 1614 that the plan for a "common dispensatory to be kept in the apothecary shops" was mentioned again in the Annals. From then on the project developed rapidly. On the thirtieth of September 1617 the president of the Royal College of Physicians of London, Dr. Atkins, told the Fellows that the Pharmacopœia was "on the point of completion."[2]

Under date of May 7, 1618, the long-expected book appeared. Apparently the demand was so urgent that the printer sold a part of the issue before the King's proclamation of April 26, which declared the Pharmacopœia obligatory for all of England, was delivered to the printer and could be included in the book.

The only copy of the May issue of the London Pharmacopœia 1618 hitherto discussed in the literature concerned (*i. e.*, that preserved in the British Museum) belongs to this part of the issue. It does not contain the King's proclamation. The page concerned is left blank, while another copy acquired by the late Charles LaWall and now in the library of the Philadelphia College of Pharmacy and Science, and a third one in the Historical Library of the Yale University School of Medicine, bear the royal manifesto.[3]

The sale must have gone on fairly well when something without precedent and without repetition in the history of European pharmacopœias happened. The work was called in to be recast. "Within four months (namely on 5th September following) arrangements were made for a new edition, which appeared on the 7th December, 1618."[4] The Pharmacopœia of May 7, 1618, was the first edition in fact; that of December 7 of the same year became the "first edition" by dictum.

There is one official explanation of these remarkable happenings in the form of an epilogue to the second issue directed to the reader of the book. This epilogue, translated from the Latin, reads as follows:

"We now edit the London Pharmacopœia in a second endeavor, with more fortunate result. We (I say) edit. For that previous unformed as well as deformed [book], may we say the hasty printer has edited it? On the contrary he hurled it into the light. As a blaze flares up from a fire and in a greedy famine deprives the stomach of its still unprepared food, so the printer snatched away this little work not yet finished off from our hands, without consulting the president, yea even during a time when the latter, who took care of corrections and polishing most thoroughly, was out of town because of a call. After his return the president found with indignation the concoction which had crept into publicity defiled with so many faults and errors, incomplete and mutilated because of lost and cut off members. Having convened his colleagues in his home, the president has called in the whole work to which he had devoted so much care for recasting and has matured a new edition. Now this book finally appears purer as to faults and more complete as to remedies. Its future is to be the more fortunate if your confidence and benevolence will support it."

This epilogue forms the basis of all later explanations in the literature of the withdrawal of the first issue of the London Pharmacopœia and its replacement by another. Munk writes that the issue of May 7, 1618, was published "surreptitiously and prematurely, by the printer in the absence of the President."[4]

C. J. S. Thompson and A. C. Wootton deal

Presented to the Section on Historical Pharmacy, AMERICAN PHARMACEUTICAL ASSOCIATION. Excerpt from pharmacopœia reproduced through courtesy of State Historical Society of Wisconsin.

in more detail with this unfortunate printer.

Thompson makes the following statement:

"The printer E. Griffin at the sign of the 'White Lily' was therefore admonished and, the publication being taken out of his hands, it was reissued on December 7th of the same year, with the errors corrected, by John Marriott at his shop in Fleet Street."[5]

A. C. Wootton writes: "This presumptuous printer was one John Marriott, at the inappropriate sign of the White Lily, *in platea vulgo dicta* Fleet Street."[6]

The statements of Wootton as well as of Thompson are misleading.

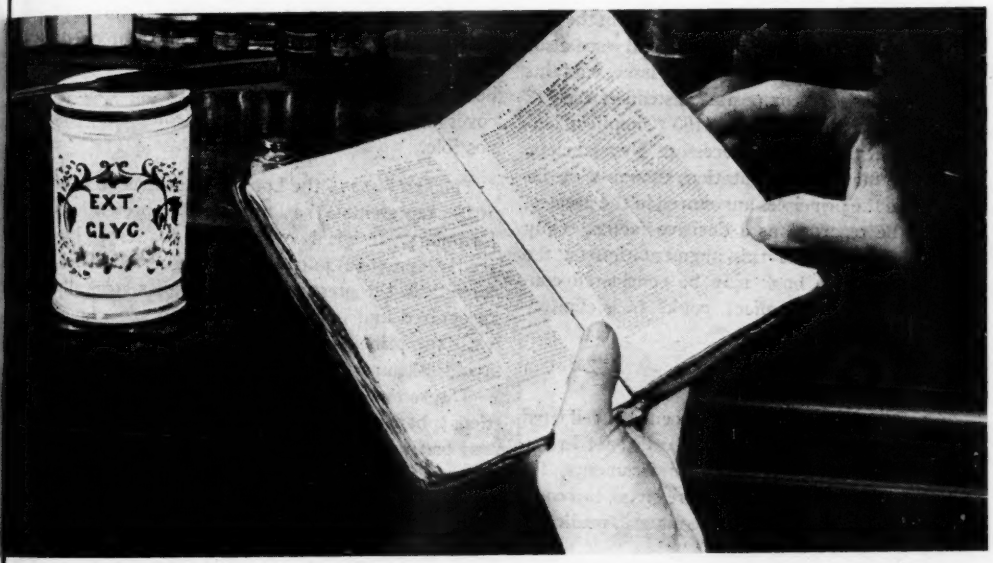
The title page of the first issue tells that Edward Griffin printed the book "*sumptibus* Joannis Marriot", *i. e.*, at John Marriot's expense. The title page of the second issue does not mention the name of the printer but merely states "printed for John Marriot." Thus it is evident that J. Marriot was the publisher of both issues.

real reason of its withdrawal. Even a very casual comparison of the two issues reveals differences of a very essential and by no means merely typographical nature.

In consequence of such a casual comparison, the author of an unsigned editorial in the well-known British journal, *The Chemist and Druggist*, remarked:

"It may well be that the prefaces to the two volumes . . . furnish another instance [other than that officially given] of the proverbial antipathy between May and December."[8]

Translation of the prefaces to the two volumes, from the Latin of the original into English, proved that there were no substantial differences. Besides a few editorial changes the preface of the first issue was literally taken over into the second book, a procedure quite consistent with the evident intention of the epilogue not to admit fundamental changes to be in existence and



He turned the job of printing of the first issue over to Edward Griffin whose printing shop enjoyed a good reputation[7] and it is by no means impossible that Griffin also printed the second issue though, because of the ominous epilogue, anonymously.

Statements in the literature as to the punishment of the printer (publisher) of the first issue of the London Pharmacopœia 1618 having proved to be incorrect, it seemed the more questionable whether indeed the technical defects were the to have been the reason for the second issue.

Hence, the decisive question was whether there were such fundamental changes and if so whether they, perhaps in connection with some facts of minor importance, could be regarded as the real reasons for the preparation of the second issue of the Pharmacopœia Londinensis 1618.

To get this question answered and to really unveil the mystery about the first official English pharmaceutical standard, a thorough comparsion of both issues not only had to be made, but the

scientific and general background had to be investigated. It seemed finally necessary to gather as much information as possible about the persons who might be regarded as responsible for the preparation of the two different issues.

It was at the initiative of my late friend Dr. Edward Kremers who had provided photostatic copies of both issues from the British Museum some years ago, and with the financial support of the Hollister Pharmaceutical Library Fund of the State Historical Society of Wisconsin, that I carried through the investigations mentioned.

The results thereof together with a facsimile reprint of the first issue of the London Pharmacopœia 1618 have just been published in book form.*

As pointed out, the preface to the first issue is, without any substantial change, taken over into the second book. In this preface the authors state clearly their intention to replace the "confusing abundance" of older formularies by a book that is "neither obviously lacking in medicaments nor crammed with them."

This intention has been fully realized in the first issue. Can that be said of the second issue also? In fact, it cannot. The second issue contains 963 formulas for "composita" instead of the 712 of the first issue and lists 1190 "simplicia" instead of the 680 of its predecessor. Nevertheless, the mere fact of augmentation, though a deviation from the principles announced in the preface, cannot be regarded as a decisive factor. Only an obvious effect of this augmentation on the character of the book may be considered conclusive. Such an effect could be definitely proved.

1. *The Simples*

(*a*) The list of simples has been changed from an enumeration of those drugs called for in the preparation of compounded medicaments, for which formulas and directions are given, to a comprehensive survey of the entire materia medica of crude drugs in common use at that time. Not only was the title of this catalog of simples changed accordingly, the list became an important source of general information. Consequently, it was taken from the rear of the book and placed before the formula part thereof.

(*b*) In addition to the increase in the number of simples, several new features have been introduced, namely synonyms and permissible surrogates. From the number of such additions the intention becomes apparent to supply an informative survey, not merely to catalog the simples required to make the composita.

2. *The Compounded Remedies*

(*a*) Not only has the number of formulas been increased considerably in the second issue, but again and again the authors refer to further preparations "omitted intentionally."

(*b*) The part devoted to formulas is interspersed with explanations, suggestions, references and even definitions.

(*c*) An increase in the number of chemical preparations is further evidence of the general tendency toward completeness.

3. *Chapters of a General Character*

(*a*) Extracts and vegetable salts: Although only a general method of preparation is given in both issues for extracts and vegetable salts, the number of examples was augmented in the second issue.

(*b*) Interpretations of generic terms: In the first issue the interpretation of generic terms is restricted to those most commonly employed. In the second issue these interpretations have been greatly extended and reveal the intention to cover the entire field just as completely as possible.

The *first issue* of the London Pharmacopœia of 1618 represents the type of unpretentious formulary designed exclusively to serve immediate practical purposes and to guarantee uniformity in the preparation of remedies generally recognized and in common use. In accordance with the principles laid down in the preface, it avoids all superfluity.

The *second issue* represents the more pretentious pharmacopœial combination of formulary and textbook, with the purpose of giving general information and also a survey of the entire materia medica, ***simplicia*** and ***composita***. Contradicting the principles laid down in the preface, it is replete with that superfluity which the authors of the first issue had condemned as "the disease to be counteracted."

There can no longer be any reasonable doubt that the withdrawal of the first issue was due

REPRODUCTION of first page of section on purgative pills in London Pharmacopœia, 1618.

* The excellent reproduction of the Pharmacopœia Londinensis together with a full report of Dr. Urdang's investigation of its unusual history is available from Schuman's, 20 E. 70th St., New York 21, at $12.—THE EDITOR.

PILVLAE PVRGANTES LENIORES SINE SCAMMONIO AVT COLOCYNTHIDE &c.

PILVLÆ ALEPHANGINÆ SIVE AROMATICÆ, *MES.*

℞ Cinnamomi.
Caryophyllorum.
Cardamomi.
Nucis Moſchatæ.
Macis.
Calami Aromatici.
Carpobalſami, aut ſem. Angelicæ.
Schœnanthi.
Ligni Aloes.
Santali Citrini.
Roſarum rubrarum.
Abſinthij ſicci ana. vnciam dimidiam.

Hæc craſſiuſculè trita, macerentur per horas duodecim in aquæ libris quatuor. deinde igne lento bulliant ad tertiæ partis abſumptionem. In colatura nutriatur
Aloes libra vna.
Tum abſumpta aquea humiditate ſuper cineres calidos, aut in hypocauſto adde
Myrrhæ.
Maſtiches ana. vnciam dimidiam.
Croci drachmas duas.
Syrupi de Abſinthio q. ſ.
fiat Maſſa ſ. a.

PILVLÆ DE ALOE LOTA.

℞ Aloes lotæ cum ſucco Roſarũ pallidarum vnciam vnam.
Agarici Trochiſcati drachmas tres.
Maſtiches drachmas duas.
Specierum Diamoſchi dulcis drachmam dimidiam.
Syrupi è roſis pallidis q. ſ.
fiat Maſſa ſ. a.

to the victory of one principle over another, not to technical deficiencies of the doomed book. The tale of the "presumptuous printer" who was blamed for the "surreptitious and premature" publication of the manuscript which had "not yet [been]finished off" may be added to the long list of similar purposeful pretexts so well known to history.

Who Were the Victors?

The victory of a different principle being a proved fact, the question has to be answered: who were the victors; who were the men who prepared the London Pharmacopœia of December 7, 1618, or were at least responsible for it?

There are differences between the two issues which are of a definitely personal character. Among the many formulas of the first book to which author names are added, are three with the names of older members of the College attached to their titles. In the second issue these names are the only names omitted. Of the members of the Royal College of Physicians of London whose names were included in the first issue, only four carried titles designating them as physicians associated with royalty in one official capacity or other. In the second issue, five additional persons were thus distinguished. In addition, the seven members acting as electors were thus designated.

It is understood that the younger generation was most opposed to every kind of discrimination, which of necessity was to the advantage of the older members of the College. This group was naturally interested in a change. Such a change could be brought about only by the withdrawal of the first issue and its replacement by another.

Nevertheless, these personal grievances—as much as they may have mobilized the individuals concerned—would not have been effective without a general dissatisfaction with the character of the work of the older generation.

This assumption may find its confirmation and explanation in the change from the Renaissance to the Baroque spirit which was taking place at that time. Revived antique simplicity was giving way to abundance and even superfluity. Effective display, not immediate practical objective, dominated mind and action. Influenced by this new trend, the younger generation may well have been disappointed by the simplicity of the first issue of the London Pharmacopœia 1618. They certainly missed formulas which they were in the habit of prescribing. But they may have missed professional display even more. It is not impossible that they considered the absence of the display of knowledge as an affront to the dignity of the Royal College of Physicians, their illustrious society.

It is understandable that neither of the two parties within the College wanted the differences between them, leading to the issue of the second book, to become obvious. That would have been detrimental to the authority of the College, hence to all of its members. In all probability it is for this reason that the preface remained unchanged, that the fundamental changes in the second issue have found no official mention whatsoever, and that the famous epilogue to the book of December 7, 1618, represents so definite an attempt at letting the typographical errors, etc., of the first issue appear to be the sole reason for its replacement.

As far as the sources available permitted, the mystery about the London Pharmacopœia 1618, prevailing for more than three centuries, has been unveiled. However, the investigation has not been restricted to this point only. The attempt has been made to determine and to explain the medico-pharmaceutical situation around 1600 and the place of the first official English pharmaceutical standard within this situation.

Of the results of this part of the investigation only one may be mentioned here. Both issues list in the catalog of simples a considerable number of animals, parts of animals and excrements—a total of 57 in the first book and 193 in the second. Wherever the London Pharmacopœia 1618 has been commented upon since the middle of the eighteenth century (these comments were always devoted to the second issue), it was with deprecatory criticism because of the abundance of nauseous drugs and especially of excrements listed.

In fact there is little reason for such an attitude. As the investigation showed, most of the animals, parts of animals and excrements concerned are taken from Dioscorides' *De Materia Medica*. Furthermore, none of the excrements listed has been prescribed for an internal compounded remedy. Of the urines, which are listed in the second issue exclusively, not a single one enters into the compounded remedies of the Pharmacopœia, either for internal or external use.

Thus it becomes apparent that the criticism mentioned is a typical example of injustice based on the standards of a later period.

With all its abundance and its peculiar eloquence the second issue of the London Pharmacopœia 1618 is charmingly representative of the

rhetorical spirit and phraseology that followed the Shakespearean (Elizabethan) period and which, with few exceptions, dominated European literature for a century.

REFERENCES

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2. *Ibid.*, III, p. 374.
3. For information about the copy owned by the Philadelphia College of Pharmacy and Science the author is indebted to Dr. John N. McDonnell, for information about the copy in the Cushing Collection at Yale to Dr. John Fulton.
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5. Thompson, C. J. S., "The Mystery and Art of the Apothecary," Philadelphia, 1929, p. 142.
6. Wootton, A. C., "Chronicles of Pharmacy, II," London, 1910, p. 61.
7. Plomer, Henry R., "A Dictionary of the Booksellers and Printers Who Were at Work in England, Scotland and Ireland from 1541 to 1667," London, 1907, p. 86.
8. *The Chemist and Druggist*, 106, 797 (1927).

SOME PROSPECTIVE MEDICAL USES OF ATOMIC ENERGY

by WILLIAM F. BALE

UNIVERSITY OF ROCHESTER, SCHOOL OF MEDICINE AND DENTISTRY

AT THE University of Rochester the peacetime application of controlled atomic energy to medicine is not considered something that will first require five, ten or twenty years of technological research as is likely true in the peacetime industrial use of atomic power. Rather, in this field, materials which can now easily be rendered available from the Manhattan Project have been sought and the possibilities of their use eagerly anticipated over a period of several years.* Their immediate application is so certain that it can be predicted with considerable assurance that it is by advances in therapeutics, in medical science, in biology, and in chemistry that the greatest peacetime rewards will be associated directly with the next ten years of the "atomic age."

Chain-reacting Uranium Piles, such as those located at Hanford, are sources of neutrons and other radiations equivalent to more than a million cyclotrons. It is these neutrons that are used to produce the new element Plutonium, an explosive component of the atomic bomb. But these same neutrons may also be used to produce in quantity long-lived radioactive carbon and hydrogen. These elements will make possible, for the medical research worker, the labeling with radioactivity of those organic compounds that play essential roles in the animal and human body, both in health and disease. Almost every organic chemical entity of possible concern in biology or medicine contains one or both of these elements in key structural positions. This means that by the proper chemical or, if necessary, biological synthesis it will be possible to obtain most organic compounds of medical or biological interest with radioactive labels.

To one acquainted with medical research, some evaluation of the possibilities opened by this work may be gained by a consideration of the vast amount of work done and useful information accumulated by work with radioactive elements hitherto available: radio-phosphorous, iron, sodium, iodine, strontium, sulfur and potassium being the most prominent. None of these elements is comparable in its usefulness to radiocarbon or hydrogen in the field of medical research, since each one is usually absent or only loosely attached to the key structural groups of most organic compounds.

At Rochester the Physics Department cyclotron has for eight years been producing other artificially radioactive and therefore labeled atoms for medical research. The extent of their use may be indicated by the more than two hundred scientific papers in which the results of investigations with labeled atoms have been reported. But now the availability of that key element, carbon, in radioactive form, hitherto known only in traces produced by the cyclotron, opens the whole field of organic compounds to the tracer technique.

Radioactive carbon will have important applications in cancer research, in pharmacology, in biology, in medical therapeutics and in medicine in general. There is one other field in which its use is likely to be of outstanding importance. Most of the triumphs of modern medicine have

* In addition to conducting extensive medical experiments over a number of years with radioactive tracer elements produced by the cyclotron, the University of Rochester has, for the past two years, investigated health hazards and protective measures for workers on nuclear fission. Dr. Stafford L. Warren, chief of the University's department of radiology, has headed the medical section of the Manhattan engineer district.—THE EDITOR

occurred in the treatment of acute infectious processes and in the advance of surgical techniques. In contrast, comparatively little is known concerning methods of delaying that gradual impairment of body functions that we describe as aging, or about combating the degenerative diseases that so often develop even in middle age or comparative youth. With better control of childhood and acute infectious diseases, chronic degenerative changes of the heart, blood vessels and kidney, together with cancer, account for higher and higher portions of reported deaths; while arthritis, seldom killing by itself, is a major cause of disability and crippling.

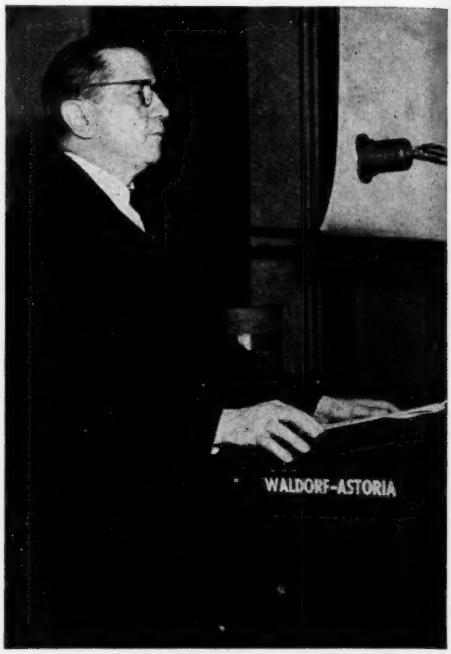
Research in these difficult fields has lagged, perhaps because of the more spectacular and easily made triumphs in other fields of investigation. It seems fair to say that a very large portion of the basic research on aging and the degenerative diseases remains yet to be done. We still need to know fundamental things such as how much of a cell is formed permanently during its early development, and what portion is renewed from metabolites supplied by the blood stream. We need to know what factors are important in cell and tissue regeneration and whether we can influence its speed and magnitude in any way. How do the different types of tissue cells in an aging animal differ in their metabolism from cells of the young and early adult animal?

In the rat, an animal that grows continually during its life span, reduction in food intake leads to a very significantly longer life, and much later onset of degenerative changes. Do we have here a clue to prolonging the life of other mammals including man? Comprehensive metabolic studies using tracer techniques should provide a basic foundation of knowledge from which it may be possible to obtain an insight leading to an increasing human adult span of productivity and pleasant existence. These new tools are of such fundamental importance that they will soon see nation-wide and world-wide use.

THIOURACIL REPRINTS

Reprints of the collaborative report on thiouracil, which appears elsewhere in this issue, are available. Send a copy to each of your physicians with an announcement that the drug is in stock. Up to five reprints without charge on request to THIS JOURNAL (additional copies five cents each). Please enclose stamped envelope.

N. F. CHAIRMAN ADDRESSES MEETING OF MANUFACTURERS



Dr. Justin L. Powers, chairman of the N. F. Committee and director of the A. PH. A. laboratory, is shown above addressing the meeting of the American Pharmaceutical Manufacturers' Association in New York. Plans for the eighth edition of the National Formulary call for publication this spring, he announced, and more than 85% of an estimated 800 pages is now in galley proof.

In revising the official compendia, Dr. Powers indicated that every effort has been made to bring about uniformity between the N. F. and U. S. P. in general features which both books have in common.

Pointing out the trend toward greater use of the metric system, he mentioned that the new N. F. will emphasize this system by printing metric doses in boldface type, followed by approximate equivalents in the apothecaries system in parentheses and less prominent type.

In addition to some 80 unofficial drugs to be newly admitted to the N. F., 102 drugs now official in the U. S. P. will be included in N. F. VIII. Since the deletion of a drug from the Pharmacopœia does not mean that it immediately becomes obsolete, it is usually desirable and even essential, Dr. Powers pointed out, to continue to provide official standards.

NEW AND NONOFFICIAL REMEDIES

recently accepted by the

COUNCIL ON PHARMACY AND CHEMISTRY, AMERICAN MEDICAL ASSOCIATION

Council descriptions of drug products are published regularly in This Journal as they are accepted. Rules upon which the Council bases its action appeared in the November, 1945 issue (6: 329, 1945) and may be secured in pamphlet form upon request to the Secretary, Council on Pharmacy and Chemistry, American Medical Association, 535 N. Dearborn St., Chicago 10.

SULFATHIAZOLE (See New and Nonofficial Remedies, 1945, p. 202).

The following dosage form has been accepted:

VOGEL LABORATORIES, MOHEGAN LAKE, N. Y.

Emulsion Sulfathiazole 5% and 10% Sterilized: 50 cc. and 200 cc. bottles. A 5 per cent or 10 per cent suspension of sulfathiazole in an emulsion of beeswax, liquid petrolatum, triethanolamine and water.

STAPHYLOCOCCUS TOXOID (See New and Nonofficial Remedies, 1945, p. 565).

The following dosage form has been accepted:

AYERST, MCKENNA & HARRISON, LTD., NEW YORK

Staphylococcus Toxoid: 3 cc. vials containing in each cubic centimeter the toxoid derived from 20,000 necrotizing doses of toxin. Preserved with 1:20,000 merthiolate.

PENICILLIN (See New and Nonofficial Remedies, 1945, p. 214).

The following additional dosage forms have been accepted:

MERCK & CO., INC., RAHWAY, N. J.

Penicillin Sodium: Vials containing 200,000 Oxford Units.

Penicillin Calcium: Vials containing 200,000 Oxford Units.

SULFADIAZINE (See New and Nonofficial Remedies, 1945, p. 185).

The following dosage form has been accepted:

VOGEL LABORATORIES, MOHEGAN LAKE, N. Y.

Emulsion Sulfadiazine 5% Sterilized: 50 cc. and 200 cc. bottles. A 5 per cent suspension of sulfadiazine in an emulsion of beeswax, liquid petrolatum, triethanolamine and water.

DIPHENYLHYANOTIN SODIUM (See New and Nonofficial Remedies, 1945, p. 528).

The following dosage form has been accepted:

PREMO PHARMACEUTICAL LABORATORIES, INC., NEW YORK

Capsules Diphenylhydantoin Sodium: 0.03 Gm. and 0.1 Gm.

THEOPHYLLINE ETHYLENEDIAMINE (See New and Nonofficial Remedies, 1945, p. 388).

The following additional dosage form has been accepted:

ERNST BISCHOFF COMPANY, INC., IVORYTON, CONN.

Solution Aminophylline: Ampuls 0.24 Gm. in 10 cc. and 0.48 Gm. in 2 cc.

BACTERIAL VACCINE MADE FROM HEMOPHILUS PERTUSSIS.—Pertussis vaccine.—Whooping cough vaccine.—A sterile suspension of killed pertussis bacilli (Hemophilus pertussis) of one or more strains showing the characteristics of phase I as described by Leslie and Gardner. The suspension is contained in isotonic solution of sodium chloride or other suitable diluent. The vaccine may be dispensed as a simple suspension, commonly known as "plain vaccine," or as an alum precipitated or aluminum hydroxide adsorbed suspension. The vaccine shall contain in each cubic centimeter not less than 10 billion organisms. The vaccine may be dispensed by itself or in combination with one or more other antigens, provided the combination does not lessen the antigenic value of the pertussis vaccine or otherwise make the product unsuitable for human use.

Actions and Uses.—Well-controlled field studies indicate that pertussis vaccine possesses sufficient antigenic value to afford considerable protective value against whooping cough. The effect in lowering the death rate is even more striking than its effect in preventing an attack of the disease, since cases do occur in spite of the previous injection of vaccine, but such cases are usually less severe.

Dosage.—The most satisfactory dose has not been established adequately. In general, the vaccine when used as a plain vaccine should contain not less than 15 billion organisms per individual injection, with the total dose representing at least 45 billion, preferably much more. When used as precipitated vaccine the individual injection should contain not less than 10 billion organisms, with a total dose of 30 billion or more organisms. Pending more com-

plete knowledge it is suggested that the user be guided by the dosage recommendation given on the manufacturer's product, since this represents the dosage accepted by the investigators whose methods have been used in preparing the vaccine.

CUTTER LABORATORIES, BERKELEY, CALIF.

Pertussis Vaccine Phase I Concentrate: 5 cc., 20 cc. and 50 cc. vials. H. pertussis 20,000 million per cubic centimeter. Preserved with phenol 0.25 per cent and merthiolate 0.002 to 0.005 per cent.

THE NATIONAL DRUG COMPANY, PHILADELPHIA

Pertussis Vaccine (Double Strength): 6 cc. vial (one immunization), 12 cc. vial (two immunizations) and 25 cc. vial (four immunizations). H. pertussis 20,000 million per cubic centimeter. Preserved with merthiolate 1:10,000.

SHARP & DOHME, INC., GLENOLDEN, PA.

Pertussis Bacterin "H" Strength: 5 cc. and 20 cc. vials. 20,000 million H. pertussis per cubic centimeter. Preserved with phenol 0.5 per cent.

THE UPJOHN COMPANY, KALAMAZOO, MICH.

Pertussis Vaccine (Single Strength): 24 cc. vials. 20,000 million H. pertussis per cubic centimeter. Preserved with phenol 0.5 per cent.

Pertussis Vaccine (Double Strength): 5 cc. and 20 cc. vials. 20,000 million H. pertussis per cubic centimeter. Preserved with phenol 0.5 per cent.

PERTUSSIS VACCINE ALUM PRECIPITATED.—A bacterial vaccine prepared from alum precipitated, killed H. pertussis.

Actions and Uses.—Same as Bacterial Vaccine made from H. pertussis.

Dosage.—Three 1 cc. subcutaneous injections of 10,000 million or 15,000 million H. pertussis at three to four week intervals.

THE NATIONAL DRUG COMPANY, PHILADELPHIA

Pertussis Vaccine (Alum Precipitated): 3 cc. vial (one immunization) and 10 cc. vial (three immunizations). 10,000 million H. pertussis per cubic centimeter. Preserved with merthiolate 1:10,000.

PERTUSSIS VACCINE COMBINED WITH DIPHTHERIA TOXOID.—A combination of pertussis vaccine with diphtheria toxoid.

Actions and Uses.—Employed in the simultaneous immunization of susceptible persons against diphtheria and whooping cough.

Dosage.—Three doses of 1 cc. at three to four week intervals.

THE NATIONAL DRUG COMPANY, PHILADELPHIA

Diphtheria-Pertussis Combined Vaccine (Alum Precipitated): Three 1 cc. vials (one immunization) and three 5 cc. vials (five immunizations). 10,000 million H. pertussis, 0.5 cc. diphtheria toxoid immunizing dose. Preserved with merthiolate 1:10,000.

SHARP & DOHME, INC., GLENOLDEN, PA.

Diphtheria-Pertussis Antigens Combined (Alum Precipitated): 10 cc. vials (three three-dose immunizations). 10,000 million H. pertussis diphtheria toxoid immunizing dose. Preserved with phenol 1:50,000.

PERTUSSIS VACCINE COMBINED WITH DIPHTHERIA AND TETANUS TOXOIDS.—A combination of pertussis vaccine with diphtheria toxoid and tetanus toxoids.

Actions and Uses.—Employed in the simultaneous immunization of susceptible persons against whooping cough and diphtheria.

Dosage.—Three subcutaneous injections of 1 cc. at three to four week intervals.

THE NATIONAL DRUG COMPANY, PHILADELPHIA

Diphtheria-Tetanus-Pertussis Combined Vaccine (Alum Precipitated): Three 1 cc. vials (one immunization) and three 5 cc. vials (five immunizations). 10,000 million H. pertussis, diphtheria toxoid and tetanus toxoid 0.33 cc. each per cubic centimeter. Preserved with merthiolate 1:10,000.

REPORT OF COUNCIL ON PHARMACY AND CHEMISTRY

PREPARATIONS EXEMPT FROM COUNCIL CONSIDERATION.—The following official preparations have been declared exempt from Council consideration for inclusion in New and Nonofficial Remedies, as their actions, uses and nature are sufficiently well understood by physicians not to require such inclusion.

This list has been adopted for publication so that it may be brought to the attention of all manufacturers and other interested groups. From time to time there may be added other drugs, the names of which will also be published.

Iron and Ammonium Citrates
Ferrous Sulfate
Calcium Gluconate
Antimeningococcic Serum
Liver and Stomach Preparations included in U. S. P.
Digitalis Preparations included in U. S. P.
Acetylsalicylic Acid
Caffeine with Sodium Benzoate
Carbon Dioxide
Oxygen
Oxygen-Carbon Dioxide Mixtures
Chlorinated Paraffin (Chlorocosane)
Cinchophen
Neocinchophen
Dextrose Solution
Sodium Chloride Solution
Isotonic Solution of Three Chlorides
Sodium Citrate
Sodium Biphosphate
Magnesium Sulfate
Trioxymethylene (Paraformaldehyde-U. S. P. X)
Methylene Blue
Quinine and Urea Hydrochloride
Salicylic Acid
Sodium Salicylate
Natural Oil of Sweet Birch (Methyl Salicylate)
Pentobarbital Sodium
Papaverine Hydrochloride
Emetine Hydrochloride
Totaquine
Tribasic Calcium Phosphate
Magnesium Trisilicate
Tribasic Magnesium Phosphate
Ichthammol Preparations
Strophanthin

A. Ph. A. Branches

PHILADELPHIA—The branch sent telegrams of protest to President Truman and the Civil Service Commission concerning the low standards which had been announced for eligibility to pharmacy positions in the government, and the text was read to members at the November meeting.

C. S. Brinton, retired chief of the Philadelphia Station of the Food and Drug Administration, was the guest speaker. He reviewed the development of food and drug regulation, both state and national, concluding with a discussion of present legislation.

CANAL ZONE—Secretary Cady announced that membership invitations had been extended to several pharmacists on the isthmus who were not yet associated with the branch. Plans were discussed to hold a future meeting at the leper colony of Palo Seco, where arrangements would be made to have a physician conduct the members through the institution.

PHILADELPHIA—Dr. John C. Krantz, Jr., of the University of Maryland School of Medicine discussed "The Mechanism of Action of Certain Anti-infective Drugs" at the December meeting.

A letter received at national headquarters from President Mitchell of the U. S. Civil Service Commission replying to objections to Announcement A-404 was read and discussed. A motion was passed expressing dissatisfaction with Mr. Mitchell's statement and offering help to the parent organization to rectify the situation. Letters were also authorized to be sent to the Surgeon General of the Army requesting action in keeping with the spirit and the letter of the Pharmacy Corps Act.

For the professional relations committee, Dr. Blythe gave a résumé of papers to appear in the *P. A. R. D. Bulletin* and *Philadelphia Medicine*.

WESTERN NEW YORK—About a hundred pharmacists attended the joint dinner session of the A. Ph. A. branch and the Western New York Retail Druggists Association. Alexander Fisch of the State Department of Labor presented an interpretation of the new Retail Trade Minimum Wage Standard Order, which affects women and minors employed in pharmacies. Frank Smith, supervisor of the N. Y. State Bureau of Narcotic Control, discussed phases of narcotic dispensing in the retail pharmacy.

ST. JOHN'S COLLEGE—Members at the November session heard Frederick D. Lascoff, a leading pharmacist and president of the New York A. Ph. A. branch, express his conviction that today's trend is toward more professional operation of retail pharmacies. Emphasizing the importance of keeping up with modern trends, Dr. Lascoff urged the students to read their professional journals regularly after graduation.

Dr. Raubenheimer introduced the speaker, and Miss Wassily, vice-president, presided over the meeting.

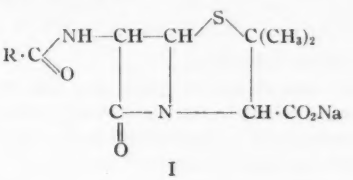
At a business session the following week the College freshmen were invited to join the A. Ph. A. and Dr. Raubenheimer reviewed the current activities of the parent organization and the accomplishments of its nearly one hundred years of professional service.

PURDUE UNIVERSITY—Student membership has increased from 30 to 85, and the branch has scheduled a number of events, both social and educational, for the year. New officers for 1946 are Gene Yoder, president; Virginia Reynolds, vice-president; Steve Sielski, treasurer; and LaVonne Anson, secretary.

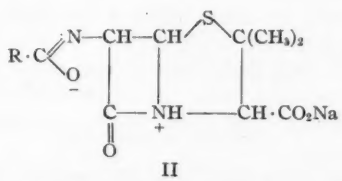
JOINT REPORT PUBLISHED ON CHEMISTRY OF PENICILLIN

A summary of the chemistry of penicillin, as revealed by experiments to date, has been published by the Committee on Medical Research of O. S. R. D. and the British Medical Research Council (*Science*, 102: 627, 1945). The several antibiotics of the penicillin class all have the empirical formula $C_9H_{11}O_4SN_2{\cdot}R$.

Present views concerning the structural formula of the penicillins have centered on a β-lactam structure (I) and an incipient azlactone grouping (II) shown below:



I



II

The preliminary information published represents collaborative studies by 17 British research groups and 21 groups in the United States.

SOME ORGANIC CHEMICALS E

by C. LEE HUYCK*

INVESTIGATIONAL work reported in this paper describes some larger-scale experiments with alcoholic solution of methyl cellulose (Tylose), polyvinyl alcohol, cetyl alcohol-mastic solution and cellulose acetate phthalate as enteric coatings for tablets. The usual in vitro disintegration test was used as the basis of judgment as to whether or not the coatings were satisfactory.

The history and literature of enteric coatings have recently been comprehensively reviewed by Thompson and Lee.[1] Reviews have also been published by Chilson[2] and Lesser[3], while developments of the past five years have been described by Volwiler and Moore,[4] Maney and Kuever,[5] Brenner,[6] Abbott and Allport,[7] Hodge, Forsynth and Ramsey[8] as well as Thompson and Lee.[9]

Volwiler and Moore[4] have patented the use of a stearic acid-phthalic anhydride-glycerol condensation product as an enteric coating for pills, capsules and tablets.

The comprehensive study by Maney and Kuever[5] covered the following points: (*a*) construction of a mechanical device for testing enteric coatings, (*b*) correlation of results of the mechanical laboratory method with results of roentgen ray examinations of the tablets in the gastrointestinal tract, (*c*) tests to determine to what extent tablets now on the market vary in disintegration time, (*d*) examination of the physiological conditions in the gastrointestinal tract to determine the type of coating which will resist the stomach fluids but disintegrate in the intestinal fluids, (*e*) development of a satisfactory enteric coating, which consisted of 68% myristic acid, 25% hydrogenated castor oil (opal wax), 2% castor oil, 1% cholesterol and 4% sodium taurocholate.

Brenner[6] tested an enteric coating solution consisting of 25 parts shellac, 5 parts castor oil and 95 parts of 96% alcohol. When the thickness of the coating was 26 to 39 microns,† the tablets began to dissolve after seven hours in artificial gastric juice and after 100 minutes in artificial intestinal juice. These results were checked in vivo by X-ray, the tablets disintegrating sixteen hours and ten minutes after ingestion. This confirms the work of others who demonstrated that the upper portion of the small intestine is slightly acid or neutral, and it takes some time for the acid of the stomach to be neutralized in the intestine.

Abbott and Allport[7] tested keratin; salol; salol–shellac; salol–benzonaphthol; salol–stearic acid–shellac; stearic acid–carnauba wax–soft paraffin–agar–elm bark; magnesium stearate-mastic; shellac; shellac–wool fat; shellac–castor oil; myristic acid–hydrogenated castor oil; cetyl alcohol; cetyl alcohol–shellac; cetyl alcohol–mastic; and cellulose acetate phthalate by an "in vitro" method.

The apparatus used was unique in that it slowly supplied fresh artificial digestive juices to the coated tablets and also moved the juices around the tablets in a manner similar to that imparted by peristaltic movement of the human gastrointestinal tract.

The cetyl alcohol–shellac and the cellulose acetate phthalate coatings proved to be the most satisfactory. Cellulose acetate phthalate gave protection in artificial gastric fluid for five hours and protection in artificial intestinal fluid for one-half hour. The cetyl alcohol–shellac coating was a solution of 10% cetyl alcohol and 10% shellac in ether. The stearic acid–carnauba wax–soft paraffin–agar–elm bark coating was satisfactory from the behavior standpoint but it required special processing with machinery not available to the retail pharmacist. A coating was considered satisfactory which would withstand the action of artificial gastric juice for five hours and

* From the Research Laboratories, Wm. S. Merrell Co.
The author is indebted to Dorothy E. Wolf of the Analytical and Control Research Laboratories, Wm. S. Merrell Co., for testing the tablets for disintegration.

† It will be recalled that a micron is one-thousandth part of a millimeter.—*Ed.*

disintegrate in the alkaline intestinal fluid within one hour.

Hodge, Forsynth and Ramsey[8] tested tablets and capsules coated with cellulose acetate phthalate and found that they possessed satisfactory enteric characteristics. In 79% to 100% of trials in human subjects, disintegration occurred in the intestine about eight hours after ingestion.

Thompson and Lee[9] studied the in vitro disintegration of enteric coated tablets from 6 pharmaceutical houses. There was considerable variation in the disintegration time of the coatings tested. It was clear that some of the coatings did not disintegrate at the proper place in the intestinal tract.

Stearic acid, mutton tallow, balsam tolu, iron bile salts, sodium taurocholate and ox bile in combination with each other were tested. A mixture of stearic acid, mutton tallow, balsam of tolu and iron bile salts and a mixture of stearic acid, mutton tallow, balsam tolu and sodium taurocholate showed the most favorable results in vitro in that they disintegrated in over five hours in acid pepsin solution and in one-half hour in alkaline pancreatin solution.

The standards set up by the authors were: (*a*) the coating should be stable to conditions in the stomach for at least five hours, (*b*) the coating should disintegrate in the intestine preferably within one hour.

Experimental

In our experiments the artificial gastric juice used for disintegration tests had the following formula:

Sodium chloride.....	1.4 Gm.
Potassium chloride.....	0.5 Gm.
Calcium chloride.....	0.06 Gm.
Hydrochloric acid, U. S. P.....	6.94 Gm.
Pepsin 1:10,000.....	0.97 Gm.
Distilled water, *q. s. ad*.....	1000.0 cc.

The formula for artificial intestinal fluid used in the disintegration tests was as follows:

Pancreatin 3X.....	0.93 Gm.
Sodium bicarbonate.....	15.0 Gm.
Distilled water, *q. s. ad*.....	1000.0 Gm.

METHYL CELLULOSE (TYLOSE).—Methylene blue tablets containing 1 gr. of methylene blue and 5 grs. of lactose were subcoated with 2 coats of 50% W/V shellac in denatured alcohol and 6 coats of 8.6% W/V gelatin solution containing 55% W/V sugar. The tablets disintegrated in twenty minutes in distilled water. Fifteen hundred of these tablets were coated with 5 coats of 10% alcoholic solution of Tylose SL5, using talc as a drying agent.

When tested for disintegration, using artificial gastric juice at 37.5° C., complete disintegration took place in about ten minutes, showing that this coating was of no value as an enteric coating for tablets.

POLYVINYL ALCOHOL.—A 10% aqueous solution of medium-viscosity polyvinyl alcohol RH 349 was found to be miscible with an equal volume of 3A denatured alcohol (alcohol U. S. P. denatured with methanol). Fifteen hundred methylene blue tablets were given 10 coats of this solution, with chalk as a drying agent, followed by 1 coat of 8.6% W/V gelatin solution containing 55% W/V sugar and 1 coat of 90.5% W/V hot sugar solution containing 20.2% W/V calcium carbonate.

The disintegration time of these tablets in distilled water was twenty minutes, showing that this coating was of no value as an enteric coating.

CETYL ALCOHOL-MASTIC SOLUTION.—Twelve coats of 10% cetyl alcohol and 10% mastic in acetone were applied to 1500 subcoated methylene blue tablets, with chalk as drying agent and a jet of cold air to speed the drying process. Hot air was not satisfactory as a drying agent since it caused the tablets to stick together.

These tablets disintegrated in artificial gastric juice in about one hour, showing that on the basis of this test the coating was of little value.

*CELLULOSE ACETATE PHTHALATE.**—Ten coats of 5% cellulose acetate phthalate in equal parts of ethyl acetate and 3A denatured alcohol were applied to 1500 methylene blue tablets, using only cold air as drying agent. The disintegration of these tablets in artificial gastric juice was one-half to one hour.

Since the results were unsatisfactory, another experiment was carried out on a smaller scale. A few of the subcoated methylene blue tablets were placed in a glass beaker and sufficient 5% cellulose acetate phthalate was added to cover the tablets. The solution was whirled occasionally and was allowed to evaporate to dryness. The disintegration of these tablets was as follows: artificial gastric juice two and one-half hours, artificial intestinal juice one-half hour, distilled water two hours.

Discussion of Results

Mills[10] tested an acetone solution of cetyl alcohol and mastic and found it to be 97.8% efficient by radiographic tests. In preparing cetyl alcohol–mastic coating solution, the ingredients

* Eastman Kodak Company, Rochester, New York.

were dissolved in acetone so that the coating could be easily sprayed on the pills or tablets. To test the efficiency of the enteric coating, barium sulfate tablets were used. The time and point of disintegration of the tablets in the alimentary canal were then determined by X-ray photographs. Ten per cent cetyl alcohol in acetone was 81.11% efficient; 10% cetyl alcohol and 10% shellac in acetone was 70.73% efficient; while 10% cetyl alcohol and 10% mastic in acetone was 97.87% efficient.

It is possible that the chalk used as a drying agent with the cetyl alcohol–mastic coating caused our unsatisfactory results when the tablets were tested by the in vitro method. Since Mills[10] used an in vivo method of measuring efficiency, the tablets coated with the cetyl alcohol–mastic solution should be tested by the same in vivo method before any opinion is expressed concerning efficiency.

From the in vitro test used, it appears that Tylose and polyvinyl alcohol are of little value as enteric coatings. With cellulose acetate phthalate good results were obtained on a small scale. This leads to the suggestion that this coating might be used by the pharmacist to give hard gelatin capsules an enteric coating. The results of larger scale experimentation were unsatisfactory in that the coating did not remain intact for any length of time in artificial gastric juice.

Summary and Conclusions

1. On the basis of in vitro disintegration tests, Tylose (methyl cellulose) and polyvinyl alcohol were found to be unsatisfactory as enteric coatings for tablets.

2. On the basis of in vitro disintegration tests, cellulose acetate phthalate has possibilities as an enteric coating but more work must be done before this material can be used satisfactorily on a large scale.

3. The cetyl alcohol–mastic coating and all the other coatings reported here should be tested by the in vivo method before any definite conclusions are drawn as to their efficiencies.

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SCHOLARSHIP PLAN OFFERED APPRENTICE BY PHARMACISTS

Interested, long-term apprentices in the retail pharmacy and assurance that funds will be available to them for pharmaceutical education is the twofold benefit from an unusual scholarship plan adopted by William J. Stigall and William P. Taggart, prescription pharmacists of Chicago.

When the two high-school youths employed in the pharmacy were sufficiently experienced to warrant an increase in salary, Mr. Taggart reports that instead of paying the prevailing wage of 60 cents per hour, the following scholarship plan was offered:

(1) Wages of $10 per week for an average of twenty hours work; (2) Two dollars per week deposited in a local bank in the name of the young man; (3) Accrued deposits and interest during high school to be used for tuition and incidental expenses for the first year at the University of Illinois College of Pharmacy; (4) Upon entering college the $2 stipend is raised to $5 per week and deposited in the local bank, accrued funds to be used for the second year of education; (5) At graduation there will be approximately $260 and interest, depending on the time the plan was initiated, which becomes the property of the young man as a graduation present; (6) If for any reason the apprentice leaves the employ of the pharmacy, one-half the funds revert to the employer; (7) If for good cause it becomes necessary to discharge the apprentice, all funds on deposit become his property; (8) The employer has first call on the services of the young man after he has received his pharmacy degree and has become licensed. It is understood that the salary offered will be that prevailing in the community. In this way a talented apprentice receives an education that otherwise might be denied him. The pharmacist himself obtains a reliable, long-term assistant and increased community good will.

Mr. Taggart passes the plan along to other pharmacists "who want to keep alive the interest young boys show in pharmacy." He and Mr. Stigall feel that the plan is a step forward in promoting interest in pharmacy as a career, and the local press recognized their endeavor.

"We have discussed the plan with the boys' parents," says Mr. Taggart, "and have their approval. We have not drawn up any lengthy legal document, but man to man have shaken hands on the plan, which they know is for their own good, although it may be readily recognized that the benefits are not one-sided."

PRESCRIPTION Information SERVICE

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GIFFORD'S BUFFER SOLUTIONS

We have a prescription calling for Solution Gifford Acid Buffer No. 2 for an eye preparation. Please send us the formula.—H. H., New York.

Gifford's Acid Buffer No. 2, which has an approximate *p*H of 6, is prepared from two stock solutions as follows:

Stock solution of sodium carbonate	0.05 cc.
Acid buffer solution No. 1	30 cc.

Mix well.

This solution is a suitable solvent for zinc salts, cocaine and epinephrine. The two stock solutions specified in the formula have the following composition:

STOCK SOLUTION OF SODIUM CARBONATE

Sodium carbonate, anhydrous	21.2 Gm.
Distilled water, previously boiled, a sufficient quantity	
To make	1000 cc.

Dissolve.

STANDARD ACID BUFFER SOLUTION NO. 1

Boric acid, crystals	12.4 Gm.
Potassium chloride, anhydrous	7.4 Gm.
Distilled water, previously boiled, a sufficient quantity.	
To make	1000 cc.

It is well to keep these two stock solutions on hand, for by combining them in various proportions buffer solutions can be prepared for any desired *p*H ranging from 5 to 9. Tables and instructions for use appear in *Pharmaceutical Recipe Book III*.

BRUSHLESS SHAVING CREAMS

Please furnish me with a formula for a brushless shaving cream. Also, where can I obtain a copy of de Navarre's Chemistry and Manufacture of Cosmetics?—J. C., Missouri.

In compounding a brushless shaving cream it is essential that a beard softener be used in conjunction with a lubricant and such bodying agents as will produce a cream of desired consistency. Two such formulas appear in *Pharmaceutical Recipe Book III*. Consistency can be adjusted by varying the amount of spermaceti if necessary. After saponification the product should be checked for excess fat or excess alkali and properly adjusted so that there is a slight excess of fatty acids.

I

Stearic acid	150 Gm.
Spermaceti	20 Gm.
Petrolatum	30 Gm.
Triethanolamine	25 Gm.
Glycerin	50 cc.
Perfume, as desired,	
Water, a sufficient quantity,	
To make	1000 Gm.

Melt the waxes and fats and heat to 70° C.

Add the triethanolamine which has been previously dissolved in the water and heated to 70° C. Stir the mixture until cooled to 40° C., and then add the glycerin and perfume.

II

Sodium borate	10 Gm.
Stearic acid	150 Gm.
White petrolatum	50 Gm.
Spermaceti	20 Gm.
Strong solution of ammonia	20 cc.
Sorbitol, syrupy	60 Gm.
Distilled water	690 cc.
Perfume, as desired,	
To make about	1000 Gm.

Melt the waxes and fats. Boil the distilled water and dissolve the sodium borate; add the strong solution of ammonia, and pour the mixture into the melted fat with constant agitation. When completely saponified add the syrupy sorbitol, stir slowly until quite cold, then add the perfume.

Maison G. de Navarre's book, *The Chemistry and Manufacture of Cosmetics*, is published by D. Van Nostrand and Company, Inc., 250 Fourth Avenue, New York City. The price is $8.

INVERTED EMULSION ADVISED

Please send me your opinion of the following and directions for compounding:

℞ *Phenol*	*gtts. xxx*
Magnesium carbonate,	
Zinc oxide, ā ā	ʒ *iv*
Olive oil	ʒ *ii*
Aqua Camphor,	
Aqua Calcis, ā ā, q. s.	ʒ *viii*

—J. L., Mississippi

When olive oil and lime water are mixed a calcium soap forms, which will in turn produce a W/O emulsion. To prepare a stable lotion, however, it is necessary to have at least 50% of oil, since this acts as an external phase for the emulsion. In your prescription we find only about 25% of oil, which is not sufficient to envelop the water phase.

Accordingly, the preferable procedure is to invert the emulsion. For lotions, the oil-emulsifying agent is Liniment of Soft Soap. If the oil is emulsified with about ½ ounce of the liniment, a smooth preparation results. Preparations of this type are usually tested by applying a small portion to the back of the hand as a check for uniformity of spread.

Incidentally, the magnesium carbonate and the zinc oxide both tend to produce W/O emulsions, and their presence makes it necessary to use more of the Liniment of Soft Soap than might otherwise be required.

STERILE LUBRICATING JELLY

What is the procedure for preparing a sterile lubricating jelly of the type given in Pharmaceutical Recipe Book III?—H. C., Ohio

Because of the instability of such products under ordinary sterilization procedures, the pharmacy in one large hospital solves the problem by incorporating bactericidal agents into the surgical lubricant, filling into sterile collapsible tubes under aseptic conditions and then testing for sterility. Their formula is as follows:

Tragacanth	400 Gms.
Locust bean gum	300 Gms.
Propylene glycol	22,700 Gms.
Boric acid	1,400 Gms.
Spirits lilac, 10%	560 cc.
Butoben	35 Gm.
Zephiran, 12.8%	15 cc.
Distilled water, to make	
	74,000 cc.

The tragacanth is covered with water and allowed to swell overnight. The propylene glycol is mixed with 18 L. of water, and in this mixture is dissolved the boric acid. The soaked tragacanth is then added to the boric acid solution and stirred with a large agitator. The Zephiran solution is added to the above mixture. The Butoben is dissolved in the spirits of lilac and also added to the mixture. Enough distilled water is then added to make the final product measure 74 L. or approximately 20 gal. The material is then passed through the colloid mill and filled into sterile tubes.

The collapsible tubes have been previously sterilized by dry heat (U. S. P. process B). The finished product must be tested for sterility. An excellent medium for this purpose is Fluid Thioglycollate Medium, Linden (available from Difco Laboratories, Detroit). This medium will reveal either aerobic or anaerobic contaminants. Use of a separate solution to inactivate the bactericidal agent for the sterility test is avoided through the action of the thioglycollate and/or sufficient dilution of the inoculum. We understand that a medium of this type will be included in U. S. P. XIII.

Science News Capsules

HYDROGEN peroxide was made in Germany during the latter days of the war by oxidation of easily oxidized organic chemicals, such as 2-ethylanthraquinone. Although production was only in the pilot plant stage, the method seems feasible for large-scale production and is simpler and less expensive than conventional electrochemical processes. Once rated "top secret" by the Germans, a report on the new process has now been issued by the Office of the Publication Board, U. S. Department of Commerce.

DDT in minute droplets of artificial oil fogs promises to be one of the most useful and economical ways of applying the insecticide for the protection of orchards, vineyards and woodlands. Early experiments with a Navy "fog generator" have led to a similar but more satisfactory sprayer for DDT, built by the Todd Shipbuilding Corp.

Arizona's famous crater, usually called Meteor Crater, wasn't caused by an enormous projectile from outer space after all. Persistent search for the supposed deeply buried meteorite merely proved it isn't there, and geologists now believe the crater was produced by a volcanic steam explosion.

A small, powerful *magnet*, the lightest ever made, is now being produced for civilian uses by sintering iron oxide and cobalt oxide.

Can the ladies really tell the difference between high-priced and inexpensive *perfumes?* Likely as not they can't, according to tests on 69 students at the University of California. In the case of lilac perfume only slightly more than half preferred the most expensive $16 brand. With gardenia, 55% preferred the fifty-cent kind to an $8 variety. With apple blossom there were a few more votes for the expensive kind—69%.

Good hunting in Texas, even in prehistoric times, was demonstrated when geologists unearthed more than 50 fossil skeletons of *giant buffalo*, much bigger than our modern bison, together with arrowheads and knives.

A vaccine for use against *canine encephalitis* has been patented by veterinarian Charles H. Beckman of St. Louis (No. 2,391,540).

Hitherto secret equipment, called the *"calutron,"* has been revealed as an electrical sorting machine that hurls atoms into a vacuum chamber and groups each kind in boxes according to weight. The apparatus was used in the isolation of uranium 235 for atomic bombs.

A special *flash-lamp* for use with a miniature camera to take color photographs of the gastrointestinal tract has been patented (No. 2,391,611) and assigned to the Gastro-Photor Laboratories Corp.

Radar pickups of flying birds, often made and correctly interpreted by both British and American observers during the war, were more bothersome to German operators. The Nazis never guessed the cause of what they termed scheinziele, or "spurious echoes," according to a German document unearthed by British investigators.

How do you make snowshoes for horses? Who can set up a child care plan in Albania? Hundreds of such improbable questions were answered for war agencies of the government by some 5000 explorers, scientists and missionaries who were rounded up to supply, through the offices of the *Ethnogeographic Board*, specialized information needed for winning the war. This unusual board has just been disbanded and a report issued on its work.

Results suggesting that para-aminobenzoic acid may possibly provide chemical aid for the first time in treating *Rocky Mountain spotted fever* were obtained in treatment of a single case by physicians from Columbia U.

A new engine for *jet-propulsion* will speed planes well in excess of 500 miles per hour, it is claimed. The motor is an axial flow turbojet engine designed for greater range and more economical operation of planes than earlier types.

Scientific discoveries can be expected to take a big spurt ahead in the next few years if the world remains at peace, Dr. Vannevar Bush predicts. Many brilliant scientists have applied themselves assiduously for five years to wartime tasks often far from their inclinations and assigned by the needs of the moment. Meanwhile, the scientist's speculative mind has not been idle, and Dr. Bush believes there is a stock of dammed-up ideas which scientists will pursue along inviting trails of research now that the war is over.

Fossil bones of a *marsupial wolf* which lived about 30,000,000 years ago has been brought from Colombia to the University of California by Dr. R. A. Stirton. Remains of several species of reptiles about 100,000,000 years old, believed hitherto un-

known to science, were also among the South American collection of fossils.

Only trained pest exterminators will be permitted to buy Monsanto's new *rodenticide*, 1080. The poison, extremely toxic to humans, is completely soluble in water and completely tasteless.

From South Africa comes word that nature anticipated man in manufacturing the basic ingredient of the rodenticide 1080. A plant bearing the Boer-Dutch name "gifblaar," or poison-blister, was analyzed by Dr. J. S. C. Marais who found that its toxicity is due to fluoroacetic acid and suggested that this acid and its compounds might be a source of valuable poisons. The natives had long been using the plant as a rat poison. American chemists made an independent discovery of the value of the same acid and its compounds without knowing of the previous South African work.

Another new *rodenticide*, alpha naphthyl thiourea, has been patented by its discoverer, Dr. Curt P. Richter of the Johns Hopkins Hospital, who has assigned rights to the government (No. 2,390,848). Experimental baitings in the Baltimore warehouse area, and elsewhere by the Army, have proved successful. The poison, called "Antu" for short, is said not to be toxic to animals other than rodents except in improbably large doses.

Fewer children are likely to be born into a family where the wife attended college than where the husband had college training. Although the reproductive rate in American families tends to decrease with advance in the educational attainment of either the husband or wife, figures compiled by the U. S. Bureau of Census show that this decrease is influenced to a greater degree by the education of the wife than by the husband's schooling.

At a recent RCA demonstration of postwar *television*, the receiving apparatus produced black-and-white pictures bright enough for easy viewing in an ordinary lighted room. Satisfactory color television is still around the corner, RCA's President Sarnoff indicated, perhaps five years away.

Common *baldness* is a sequela of sexual maturation and results in most instances from stimulation by male hormone substances, according to Dr. James B. Hamilton of the Long Island College of Medicine. This would explain why most baldness is seen in men, rather than women. Avoiding tight bands, such as hats, and massaging the scalp to stimulate circulation were debunked as measures to prevent or cure this condition. Heredity and age, however, are still considered important factors.

A dissenting note in the applause for the A. M. A.'s program for nation-wide voluntary *health insurance* was heard from the Physicians Forum in a statement which said in part: "The Physicians Forum, comprised of doctors who are all members of the American Medical Association, has spent many years of study on the subject and has come to this conclusion: Voluntary health insurance is merely an indication of what could be accomplished on a national scale if the President's proposal assuring the health of all Americans is passed by Congress. Until their recent reversal, the American Medical Association strongly opposed even this elementary device for medical care."

Further promising results have been reported from the Harvard Medical School in the treatment of *petit mal* epilepsy with 3,5,5-trimethyloxasolidine-2,4-dione. As clinical trials are not yet complete, the new drug, called Tridione for short, has not yet been released to pharmacists.

An ultra-high-speed *microtome* has been developed to section plant and animal tissues for examination under the electron microscope. Sections range from 1 micron to 0.1 micron in thickness, the thinnest section thus being only about one five-hundredth of a hair's breadth thick.

A new optical instrument, called a *Rotascope* (GE) is claimed to be the first instrument of its kind which permits continuous viewing of a rotating object at any particular point in its path of travel. For example, whirling plane propellers appear to stand still when viewed through the device.

A new *antibiotic* has been found in pure cultures of the bacterium that causes one of the most troublesome of bee diseases, American foulbrood. The discoverer, Dr. E. C. Holst of the U. S. Department of Agriculture, reports that experiments to determine possible therapeutic uses are in progress.

Neostigmine methyl sulfate (prostigmine) may turn out to be a cure for the poisonous bite of the *black widow spider*. Evidence is limited to treatment of one case at Roper Hospital in Charleston, S. C., where a single dose brought "dramatic and complete relief of muscle spasm and pain."

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Typical Days

FROM THE SECRETARY'S DECEMBER DIARY

—3rd—

FOLLOWING the customary Monday morning disposal of a very heavy mail, a lengthy conference and luncheon with Lt. Col. Nelson, one of the senior members of the Pharmacy Corps of the Regular Army who has just returned from India and is about to take an assignment in New York involving Army specifications for medical and health supplies. The experience of these Army men, who travel from India to the United States in as many hours as our forefathers took days for such trips, is highly interesting and one wonders that they come through in such healthy shape with all of the disease, lack of sanitation and inconvenience that is rampant in Mother India.

—4th—

At work with the staff on routine matters and, after a brief lunch at the desk, much preparation for several important meetings tomorrow and then to meet George Beal for dinner at the Washington Hotel, followed by an evening trip with him to the Headquarters building to confer about many plans for the New Year. Then for some "homework" before calling it a day.

—5th—

Heading the list of appointments today were representatives of certain D. C. pharmacists who are urging amendment of the Pharmacy Act to permit licensure without college graduation. Chairman Beal of the Council, unable because of weather to fly to Savannah today as originally arranged, dropped in to hear the arguments in favor of this bill which left us both unmoved and more certain than ever that the Council has taken the right position in opposing such legislation. Before luncheon came Einbeck, Frates and DuMez to discuss ways and means for implementing the desires of the Committee on Status of Pharmacists in the Government Service for action on the Pharmacy Corps in the Army and Navy. Following luncheon at the Washington Hotel this "Steering Committee" proceeded to Capitol Hill for further action, while we proceeded with the daily routine.

—6th—

This day to meet Treasurer Schaefer at Baltimore for the annual trip to the bank vault to clip coupons representing interest on the invested funds of the ASSOCIATION. Later to arrange for the investment of certain accumulated funds to the best interests of the ASSOCIATION, and this is still a matter of purchasing government bonds. Later to Washington, and after dinner discussing with Schaefer, Swain and others the program to be considered at the National Drug Trade Conference meeting tomorrow.

—7th—

Early to the office and then to the Statler Hotel for the revived annual meeting of the National Drug Trade Conference. And it seemed like old times to have the nine national pharmaceutical organizations representing the Conference sit around the table and discuss present-day problems affecting all of us. As chairman of the Resolutions Commitee there was the task of putting into words the sentiments expressed on these broad problems (elsewhere reported in this issue of the JOURNAL). Following adjournment of the Conference and a quick trip to the office to sign the mail, there came dinner at the Washington Hotel with President Moulton and long discussions far into the night about current A. PH. A. problems.

—8th—

Early to the office with President Moulton to dispose of routine business and then to receive Dr. George Urdang and his charming wife who are visitors in Washington on their way to New York. By a fortunate circumstance and with the help of Mrs. Powers and the Powers' car we were able to visit the Stabler-Leadbeater pharmacy in Alexandria and press Dr. Urdang into service for an evaluation of the stock and fixtures of this historic establishment. A pleasant and, for us, a highly instructive visit with Mr. and Mrs. Reese who have done so much through the Landmarks Association of Alexandria to preserve this historic pharmacy and who are ready to cooperate in the preservation of the pharmaceutical equipment and stock for future historical records. All in all a day well spent in splendid company and with good progress to report on a project that means much to peacetime American pharmacy of the future.

At night with Dr. Urdang at dinner at the Willard and then a long session about the future of various ventures in the field of pharmaceutical history, museum activity and international relations.

—9th—

A part of this Sunday spent with the Conference of Allied Medical Professions in the state of New Jersey, over which we have presided for a number of years and now relinquish the chair to the president of the State Nurses' Association. This project has withstood the test of time and has been a bulwark of defense against encroachment of politicians on the preserves of the professions. Later in the day to meet Justin Powers on his way from Philadelphia and after an uneventful automobile ride to Red Bank to dine and spend the night prior to a series of meetings in New York in the days to come.

—10th—

To New York for the meetings of the American Pharmaceutical Manufacturers' Association and the

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palm goes to Charles Wesley Dunn and his associates for staging a remarkable array of scientific talent in connection with the annual scientific award of the A. Ph. M. A. to the Rockefeller Foundation for Medical Research. And never has it been our privilege to listen to so many outstanding scientists report the latest advances in their respective fields in so short a space of time. Later to dinner at the Waldorf-Astoria with members of the A. Ph. M. A. and with a particularly friendly group at our table including George Moulton, Justin Powers, Joe Noh, recently made vice-president of Winthrop Chemical Company after several years of spendid service to the Army as head of the medical supplies Purchasing Division of the Surgeon General's Office in New York City, and others. Thankful for a good room at the Pennsylvania Hotel that night, shared with Dr. Powers.

—11th—

After an early breakfast a meeting of the A. PH. A. Laboratory Committee at the Pennsylvania Hotel with George Beal presiding and Messrs Taylor, Cook, Powers, and Green in attendance. A careful review of the recommendations for activities in the A. PH. A. Laboratory followed by some excellent suggestions for additions and improvements of the work at hand. In the afternoon to attend some sessions on medical care plans and other health activities, and at 6 o'clock to meet with the Joint Committee of the American Social Hygiene Association and the A. PH. A. for the annual roundup of activities in the joint effort to combat venereal disease. Heard with much pleasure the most recent statistics showing a precipitous drop in the number who offer venereal disease remedies in drugstores. It is almost to the vanishing point. All of which pleases the American Social Hygiene Association as much as it does us. Then to the Pennsylvania Hotel for the Remington Medal Dinner at which were gathered several hundred enthusiastic friends of Joseph Rosin, the 1945 Medalist.

—12th—

All morning at the Pennsylvania Hotel working on A. PH. A. problems and conferring by telephone and otherwise with Ballard, Klumpp, Corwin, Jennings Murphy and others. Secretary Murphy of the Wisconsin Pharmaceutical Association seems particularly alert to the store remodeling problems of retail pharmacists, and has some excellent ideas on the subject which will soon receive greater publicity. At 4 p.m. to the Academy of Medicine for an historic meeting to oppose the antivivisectionists who are planning to hamper medical research by fostering state and national legislation to prevent experimentation on animals. When men like Simon Flexner and A. J. Carlson come out of retirement to

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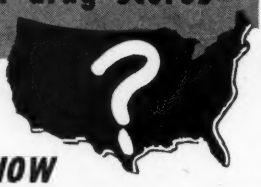

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give this movement leadership, it is plain that the scientific fraternity is aroused, and well it might be. To the Pennsylvania station for the 6:30 train to Washington which was boarded several seconds in advance of departure, and landed us at the capital late as usual, but in time to reach the hotel before midnight and still sign and mail the letters which competent staff assistants had made available during the day.

—13th—

Most of this day sitting with the Advisory Committee on Surplus Property to the Federal Security Agency discussing procedures for expediting the transfer of surplus property in the medical and health supply category to institutions, agencies and others entitled to such property in the field of health and medical care, and it is gratifying to learn that pharmacy colleges will be in a position to acquire needed laboratory equipment at reduced rates.

—14th—

Bidding good-bye at luncheon today to Joseph B. Burt who will soon succeed Dean Lyman at the University of Nebraska, and who has spent several years in Washington with WPB. He has wound up his activities at the national capital with a month and a half at A. PH. A. headquarters digesting and compiling barbiturate regulations and suggested proposals for restriction of illegitimate sale of such products; also reviewing medical care plans offered by the various states with particular emphasis on the pharmacy provisions. A job well done.

—15th—

After a morning spent at the office, which was officially closed, gathering up loose ends in preparation for a trip to the Windy City, boarded an afternoon train in time to reach home for what was left of the week end.

—16th—

In the late afternoon departed for Chicago on "The Admiral." Regardless of the name of the train, these days one can prognosticate in advance that it will arrive in Chicago too late for scheduled appointments.

—17th—

And so it was. Due in Chicago at 8:25 a.m. Time of arrival: 12:45 p.m. The usual run around at the Palmer House to obtain the "confirmed" reservation. A quick trip to the Grant Hospital and a quicker sandwich lunch, and then a splendid meeting with hospital pharmacists Hansen, Francke, Stockert, Reamer and Scott assembled to consider the activities of the growing Society of Hospital Pharmacists. Sorry to learn that Sister Mary John was unable to join the group because of illness. In an intensive review of hospital pharmacy organization future plans were developed for more complete integration of the activities of the A. S. H. P. with A. PH. A. This group recognizes how much of pharmacy's future depends on how well they meet their responsibilities. Later to dinner at the Palmer

House with Francke, Evlyn Scott and with Louise Schmitz who came from Minneapolis to conclude arrangements for joining the staff as research assistant to the A. PH. A. secretary. There followed long discussions of plans and projects, continued later with Don Francke who is, at the moment, the moving and guiding spirit of this group, and whose *Bulletin* of the A. S. H. P. is attracting wide attention.

—18th—

To the American Hospital Association with Don Francke to talk with Dr. Hullerman about plans for the Hospital Pharmacy Institute scheduled next spring at Ann Arbor under joint auspices of A. H. A., A. PH. A. and A. S. H. P., and the plans are well advanced. Then to lunch with N. A. B. P.'s Costello to discuss many a problem relating to pharmaceutical education and licensure. Next a visit with John Dargavel and then to the U. of Illinois Chicago campus for a two-hour conference with President-elect Serles before joining the 300th meeting of the Chicago Branch of the A. PH. A. at the Illinois Union. Here were gathered a most friendly group of pharmacists and their wives to listen to what good can come out of Washington, and we gave them a factual survey of A. PH. A.'s aims and objectives as of 1946. The opportunity to greet many old friends and meet new active workers was well worth the trip.

—19th—

Another conference with N. A. B. P.'s efficient secretary, and thanks to him a reservation on the "Liberty Limited" this afternoon for Washington. At lunch with Charlie O'Malley laying plans for further development of our advertising program for the JOURNALS. Then for a bit of Christmas shopping before making a dash to board the train at 3:10 p.m. Hardly a half hour out of Chicago when the first of a series of engine breakdowns occurred, so lost three hours traveling from Chicago to Valparaiso, all of which augurs well for the usual "delay, linger and wait" which seems the by-word for P. R. R. these days.

—20th—

Due in Washington 8:40 a.m. Arrived 6:30 p.m. after the worst travel experience yet recorded in these columns.

—21st—

The desk piled high after an absence of four days in place of the calculated three, but much reading done on the train which expedites the dictation but does not set the calendar back from Thursday to Wednesday.

—22nd—

After the morning in the quiet of a deserted office, fortunate enough to find one unoccupied seat on a train to New Jersey and then late in the bitter cold arriving for the Christmas holidays at home.

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